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OM protein - protein search, using sw model

Run on: January 21, 2004, 09:14:54 ; Search time 2.1109 Seconds
(without alignments)
601.551 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1107863 seqs, 158726573 residues

Total number of hits satisfying chosen parameters: 1107863

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_19Jun03:*

- 1: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
- 2: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
- 3: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
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- 20: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
- 21: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
- 22: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
- 23: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*
- 24: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2003.DAT:*

Pred. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,

and is derived by analysis of the total score distribution.

SUMMARIES

| Result | % | | | | | | |
|--------|-------|-------|-------|--------|----------|--------------------|-------------|
| No. | Score | Query | Match | Length | DB | ID | Description |
| 1 | 40 | 100.0 | 8 | 21 | AAU94772 | Beta-secretase sub | |
| 2 | 40 | 100.0 | 8 | 22 | AAE10660 | Human Aspartyl pro | |
| 3 | 40 | 100.0 | 8 | 22 | AAE06902 | Human amyloid prec | |
| 4 | 40 | 100.0 | 8 | 22 | AAU06631 | Beta secretase sub | |
| 5 | 40 | 100.0 | 8 | 22 | AAU06635 | Synthetic fluoresc | |
| 6 | 40 | 100.0 | 8 | 22 | AAU07230 | Human beta-amyloid | |
| 7 | 40 | 100.0 | 8 | 22 | AAE02612 | Human Aspartyl pro | |
| 8 | 40 | 100.0 | 8 | 23 | ABB78621 | APP Swedish mutant | |
| 9 | 40 | 100.0 | 9 | 19 | AAW82083 | Fluorogenic protea | |
| 10 | 40 | 100.0 | 9 | 21 | AAB07873 | A peptide fragment | |
| 11 | 40 | 100.0 | 9 | 21 | AAU87949 | Mammalian amyloid | |
| 12 | 40 | 100.0 | 9 | 23 | ABU60430 | Protease binding p | |
| 13 | 40 | 100.0 | 10 | 13 | AAR22054 | Peptide P1. Synth | |
| 14 | 40 | 100.0 | 10 | 13 | AAR24261 | Human amyloidin pr | |
| 15 | 40 | 100.0 | 10 | 20 | AAW82440 | Human amyloid beta | |
| 16 | 40 | 100.0 | 10 | 21 | AAU69703 | Beta-APP alpha-sec | |
| 17 | 40 | 100.0 | 10 | 22 | AAE10654 | Human wild-type AP | |
| 18 | 40 | 100.0 | 10 | 22 | AAE06899 | Human amyloid prec | |
| 19 | 40 | 100.0 | 10 | 22 | AAU06628 | Asp2 recognition s | |
| 20 | 40 | 100.0 | 10 | 22 | AAU07227 | Human beta-amyloid | |
| 21 | 40 | 100.0 | 10 | 22 | AAG62668 | Beta-sheet breaker | |
| 22 | 40 | 100.0 | 10 | 22 | AAE02606 | Human wild-type AP | |
| 23 | 40 | 100.0 | 10 | 22 | AAB66574 | Synthetic peptide | |
| 24 | 40 | 100.0 | 10 | 22 | AAB46207 | Human APP derived | |
| 25 | 40 | 100.0 | 10 | 22 | AAB46208 | Human APP derived | |
| 26 | 40 | 100.0 | 10 | 22 | AAB46209 | Human APP derived | |
| 27 | 40 | 100.0 | 10 | 22 | AAB61336 | Sythetic peptide f | |
| 28 | 40 | 100.0 | 10 | 23 | ABG78375 | Human beta amyloid | |
| 29 | 40 | 100.0 | 10 | 23 | ABG30940 | Nogo/BACE method c | |
| 30 | 40 | 100.0 | 10 | 23 | AAU99490 | Peptide #1 used as | |
| 31 | 40 | 100.0 | 10 | 23 | ABB78615 | Beta-secretase spe | |
| 32 | 40 | 100.0 | 10 | 23 | ABB06426 | Human APP beta-sec | |
| 33 | 40 | 100.0 | 10 | 24 | ABG76103 | Amyloid precursor | |
| 34 | 40 | 100.0 | 11 | 22 | AAB75143 | APP beta-secretase | |
| 35 | 40 | 100.0 | 11 | 22 | AAB75144 | Asp 1 substrate se | |
| 36 | 40 | 100.0 | 11 | 22 | AAB97468 | Asp2 substrate wil | |
| 37 | 40 | 100.0 | 12 | 22 | AAB74931 | Beta-amyloid precu | |
| 38 | 40 | 100.0 | 12 | 23 | ABB08997 | Amyloid precursor | |
| 39 | 40 | 100.0 | 12 | 23 | ABB07592 | Biotinylated synth | |
| 40 | 40 | 100.0 | 12 | 23 | AAE16657 | APP substrate pept | |
| 41 | 40 | 100.0 | 12 | 23 | AAU74831 | Synthetic amyloid | |
| 42 | 40 | 100.0 | 12 | 24 | AAO26795 | Beta-secretase sub | |
| 43 | 40 | 100.0 | 13 | 19 | AAW70869 | Beta-amyloid pepti | |
| 44 | 40 | 100.0 | 13 | 23 | AAM50891 | Fluorescent substr | |
| 45 | 40 | 100.0 | 13 | 24 | ABP71624 | Beta-secretase act | |

ALIGNMENTS

RESULT 1

AAAY94772

ID AAY94772 standard; Protein; 8 AA.

XX

AC AAY94772;

XX

DT 12-FEB-2001 (first entry)

XX

DE Beta-secretase substrate peptide SEQ ID 18.

XX

KW Beta-secretase; enzyme; amyloid plaque; Alzheimer's disease;

KW Down's syndrome; amyloid angiopathy; gene therapy; neuroprotective.

XX

OS Synthetic.

XX

PN WO200058479-A1.

XX

PD 05-OCT-2000.

XX

PF 23-MAR-2000; 2000WO-US07755.

XX

PR 26-MAR-1999; 99US-0277229.

XX

PA (AMGE-) AMGEN INC.

XX

PI Citron M, Vassar RJ, Bennett BD;

XX

DR WPI; 2000-594643/56.

XX

PT Isolated beta-secretase nucleic acids and encoded polypeptides, useful
PT for diagnosis and gene therapy of Alzheimer's disease -

XX

PS Example 10; Page 117; 145pp; English.

XX

CC This invention relates to 3 nucleotide sequences encoding beta-secretase
CC proteins. Beta-secretase is an enzyme involved in the production of one
CC of the components of amyloid plaques involved in Alzheimer's disease. The
CC invention includes an expression vector comprising the nucleotide
CC sequence, a host cell comprising the expression vector, and a process for
CC producing the protein through culturing the transformed cells. Also
CC included in the invention are a polypeptide derivative of the
CC beta-secretase protein, a fusion protein comprising beta-secretase fused
CC to a heterologous amino acid sequence, and a method for modulating the
CC levels of beta-secretase polypeptide in a mammal comprising administering
CC the polynucleotide sequence. Beta-secretase exhibits neuroprotective and
CC nootropic activity. The beta-secretase nucleotide sequence may be used to
CC map locations of the beta-secretase gene and related genes on chromosomes
CC and as hybridization probes in diagnostic assays to test for the presence
CC of beta-secretase DNA or RNA, such as in Alzheimer's disease, Down's
CC syndrome, and amyloid angiopathy. The nucleotide sequence may also be
CC used as anti-sense inhibitors of beta-secretase expression, in gene
CC therapy of Alzheimer's disease, and for the identification of compounds
CC that modulate beta-secretase activity. Antibodies to the beta-secretase
CC protein may be used for in vitro and in vivo diagnostic purposes to
CC detect the presence of beta-secretase polypeptide in a body fluid or cell
CC sample. The present sequence represents a beta-secretase substrate
CC peptide.

XX

SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 21; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8

|||||||

Db 1 EVKMDAEF 8

RESULT 2

AAE10660

ID AAE10660 standard; peptide; 8 AA.

XX

AC AAE10660;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human Aspartyl protease-1 (hu-Asp-1) beta-secretase, wild-type peptide.

XX

KW Human; aspartyl protease 1; Asp1; amyloid precursor protein; APP;
KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;
KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Cleavage-site 4..5

XX

PN GB2357767-A.

XX

PD 04-JUL-2001.

XX

PF 22-SEP-2000; 2000GB-0023315.

XX

PR 23-SEP-1999; 99US-0155493.

PR 23-SEP-1999; 99US-0404133.

PR 23-SEP-1999; 99WO-US20881.

PR 13-OCT-1999; 99US-0416901.

PR 06-DEC-1999; 99US-0169232.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2001-444208/48.

XX

PT Polypeptide comprising fragments of human aspartyl protease with
PT amyloid precursor protein processing activity and alpha-secretase
PT activity, for identifying modulators useful in treating Alzheimer's
PT disease -

XX

PS Example 15; Page 92; 187pp; English.

XX

CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified

CC Asp1 proteins which lack transmembrane domain or amino terminal
CC domain or cytoplasmic domain and retains alpha-secretase activity
CC and amyloid protein precursor (APP) processing activity. The proteins
CC of the invention are useful for assaying hu-Asp1 alpha-secretase
CC activity, which in turn is useful for identifying modulators of
CC hu-Asp1 alpha-secretase activity, where modulators that increase
CC hu-Asp1 alpha-secretase activity are useful for treating Alzheimer's
CC disease (AD) which causes progressive dementia with consequent
CC formation of amyloid plaques, neurofibrillary tangles, gliosis and
CC neuronal loss. Hu-Asp1 protease substrate is useful for assaying
CC hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein with
CC the substrate under acidic conditions and determining the level of
CC hu-Asp1 proteolytic activity. The present sequence is human aspartyl
CC protease-1 (hu-Asp-1) beta-secretase, wild-type peptide which is used
CC for determining the enzymatic activity of Asp-1 protein lacking a
CC transmembrane (TM) domain and containing (His)6 tag.

XX

SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;

Best Local Similarity 100.0%; Pred. No. 9.3e+05;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8

|||||||

Db 1 EVKMDAEF 8

RESULT 3

AAE06902

ID AAE06902 standard; peptide; 8 AA.

XX

AC AAE06902;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein (APP) substrate peptide.

XX

KW Human; aspartyl protease 2; Asp 2; beta-amyloid precursor protein; APP;

KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;

KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;

KW neuroprotective; antisense therapy; gene therapy.

XX

OS Homo sapiens.

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB00799.

XX

PR 09-MAY-2001; 2001WO-IB00799.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.
 XX
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
 XX
 DR WPI; 2001-483072/52.
 XX
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
 PT activity -
 XX
 PS Claim 128; Page 101; 185pp; English.
 XX
 CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid
 CC precursor protein (APP) isoforms and their corresponding DNA molecules.
 CC Human aspartyl proteases can act as beta-secretase proteases useful for
 CC treating Alzheimer's disease. APP isoforms are useful for identifying
 CC modulators of amyloid-beta peptide production, for use in designing
 CC therapeutics for the treatment and prevention of Alzheimer's disease,
 CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis
 CC and neuronal loss. APP isoforms are also used in methods for identifying
 CC inhibitors and modulators of human Asp2 activity. The invention relates
 CC to a method for identifying agents that modulate the activity of human
 CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used
 CC as a means to screen in cellular assays for the inhibitors of beta- and
 CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in
 CC polymerase chain reactions (PCR). The probes are useful for detecting
 CC Hu-Asp nucleic acids in in vitro assays and in Northern and Southern
 CC blots. The present sequence is human amyloid precursor protein (APP)
 CC substrate peptide related to the invention.
 XX
 SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
 Best Local Similarity 100.0%; Pred. No. 9.3e+05;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 EVKMDAEF 8
 |||||
 Db 1 EVKMDAEF 8

RESULT 4

AAU06631

ID AAU06631 standard; Peptide; 8 AA.

XX

AC AAU06631;

XX

DT 24-OCT-2001 (first entry)

XX

DE Beta secretase substrate peptide.

XX

KW Aspartyl protease; Asp2; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; Beta secretase substrate peptide.

XX

OS Synthetic.

XX
 PN WO200149098-A2.
 XX
 PD 12-JUL-2001.
 XX
 PF 09-MAY-2001; 2001WO-IB00798.
 XX
 PR 09-MAY-2001; 2001WO-IB00798.
 XX
 PA (BIEN/) BIENKOWSKI M J.
 PA (GURN/) GURNEY M E.
 PA (HEIN/) HEINRIKSON R L.
 PA (PARO/) PARODI L A.
 PA (YANR/) YAN R.
 XX
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
 XX
 DR WPI; 2001-502549/55.
 XX
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
 PT activity -
 XX
 PS Claim 88; Page 94; 185pp; English.
 XX
 CC The invention relates to a purified polypeptide comprising a fragment of
 CC mammalian aspartyl protease (Asp2) protein which lacks the Asp2
 CC transmembrane domain and the Asp2 protein, and where the polypeptide and
 CC the fragment retain the beta-secretase activity of the mammalian Asp2
 CC protein. The invention also details polynucleotides for the Asp
 CC proteins and vectors expressing them, and a polypeptide (isoform of
 CC amyloid protein precursor (APP)) comprising the amino acid sequence of an
 CC APP or its fragment containing an APP cleavage site recognizable by a
 CC mammalian beta-secretase, and further comprising two lysine residues at
 CC the carboxyl terminus of the amino acid sequence of the mammalian APP or
 CC APP fragment. Also included in the invention are methods of identifying
 CC modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are
 CC useful for treating Alzheimer's disease. APP is useful in methods for
 CC identifying inhibitors or modulators of human Asp2 activity and
 CC amyloid-beta (Abeta) peptide production. APP is also useful in designing
 CC therapeutics for the treatment or prevention of Alzheimer's disease.
 CC APP comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which
 CC is associated with increased levels of Abeta processing is useful in
 CC assays relating the Alzheimer's research. The expression vector is useful
 CC for recombinantly expressing APP. Nucleic acids that hybridise to
 CC Asp oligonucleotides are useful as probes or primers. The probes are
 CC useful for detecting Hu-Asp nucleic acids in in vitro assays and in
 CC Northern and Southern blots. The present sequence is a Beta secretase
 CC substrate peptide.
 XX
 SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
 Best Local Similarity 100.0%; Pred. No. 9.3e+05;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 EVKMDAEF 8
| | | | | | | |
Db 1 EVKMDAEF 8

RESULT 5

AAU06635

ID AAU06635 standard; Peptide; 8 AA.

XX

AC AAU06635;

XX

DT 24-OCT-2001 (first entry)

XX

DE Synthetic fluorescent Asp2 substrate.

XX

KW Aspartyl protease; Asp2; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta.

XX

OS Synthetic.

XX

FH Key Location/Qualifiers

FT Modified-site 1

FT /note= "Glu is covalently linked to a fluorescent

FT MCA moiety"

FT Modified-site 8

FT /note= "Glu is covalently linked to a fluorescent

FT K-DNP moiety"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB00798.

XX

PR 09-MAY-2001; 2001WO-IB00798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502549/55.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2

PT activity -

XX

PS Example 12; Page 81; 185pp; English.

XX

CC The invention relates to a purified polypeptide comprising a fragment of

CC mammalian aspartyl protease (Asp)2 protein which lacks the Asp2

CC transmembrane domain and the Asp2 protein, and where the polypeptide and

CC the fragment retain the beta-secretase activity of the mammalian Asp2
 CC protein. The invention also details polynucleotides for the Asp
 CC proteins and vectors expressing them, and a polypeptide (isoform of
 CC amyloid protein precursor (APP)) comprising the amino acid sequence of an
 CC APP or its fragment containing an APP cleavage site recognizable by a
 CC mammalian beta-secretase, and further comprising two lysine residues at
 CC the carboxyl terminus of the amino acid sequence of the mammalian APP or
 CC APP fragment. Also included in the invention are methods of identifying
 CC modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are
 CC useful for treating Alzheimer's disease. APP is useful in methods for
 CC identifying inhibitors or modulators of human Asp2 activity and
 CC amyloid-beta (Abeta) peptide production. APP is also useful in designing
 CC therapeutics for the treatment or prevention of Alzheimer's disease.
 CC APP comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which
 CC is associated with increased levels of Abeta processing is useful in
 CC assays relating the Alzheimer's research. The expression vector is useful
 CC for recombinantly expressing APP. Nucleic acids that hybridise to
 CC Asp oligonucleotides are useful as probes or primers. The probes are
 CC useful for detecting Hu-Asp nucleic acids in in vitro assays and in
 CC Northern and Southern blots. The present sequence is a synthetic
 CC fluorescent substrate used to assay Asp2.

XX

SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
 Best Local Similarity 100.0%; Pred. No. 9.3e+05;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 1 EVKMDAEF 8

RESULT 6

AAU07230

ID AAU07230 standard; Peptide; 8 AA.

XX

AC AAU07230;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human beta-amyloid protein precursor, APP-beta secretase site peptide #3.

XX

KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;

KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;

KW beta-secretase; Alzheimer's disease; APP-beta.

XX

OS Homo sapiens.

XX

PN WO200149097-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB00797.

XX

PR 09-MAY-2001; 2001WO-IB00797.

XX

PA (BIEN/) BIENKOWSKI M J.
PA (GURN/) GURNEY M E.
PA (HEIN/) HEINRIKSON R L.
PA (PARO/) PARODI L A.
PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502548/55.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl
PT protease 2, lacking Asp2 transmembrane domain and retaining beta
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT activity -

XX

PS Claim 88; Page 94; 185pp; English.

XX

CC The invention relates to a novel purified polypeptide comprising a
CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the
CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide
CC and the fragment retain the beta-secretase activity of the mammalian Asp2
CC protein. Also included is an isoform of amyloid protein precursor (APP)
CC comprising the amino acid sequence of a APP or its fragment containing
CC an APP cleavage site recognisable by a mammalian beta-secretase, and
CC further comprising two lysine residues at the carboxyl terminus of the
CC amino acid sequence of the mammalian APP or APP fragment. The
CC polypeptides are used for assaying for modulators of beta-secretase
CC activity; identifying agents that inhibit the APP processing activity
CC of human Asp2 aspartyl protease (Hu-Asp2); identifying agents that
CC modulate the activity of Asp2; and for reducing cellular production of
CC amyloid beta (Abeta) from APP. Agents identified by the above methods
CC are useful for treating Alzheimer's disease; and for identifying
CC modulators of amyloid-beta (Abeta) peptide production, for use in
CC designing therapeutics for the treatment or prevention of Alzheimer's
CC disease. Probes and primers derived from Asp nucleic acid sequences
CC are useful for detecting Hu-Asp nucleic acids in in vitro assays and in
CC Northern and Southern blots. The present sequence represents the
CC amino acid sequence of human amyloid protein precursor, APP-beta
CC secretase site peptide substrate #3 used in assays of human Asp2 beta-
CC secretase activity.

XX

SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;

Best Local Similarity 100.0%; Pred. No. 9.3e+05;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 EVKMDAEF 8

|||||||

Db 1 EVKMDAEF 8

RESULT 7

AAE02612

ID AAE02612 standard; peptide; 8 AA.

XX

AC AAE02612;

```

XX
DT 10-AUG-2001 (first entry)
XX
DE Human Aspartyl protease-1 (hu-Asp-1) beta-secretase, wild-type peptide.
XX
KW Human; alpha-secretase; amyloid precursor protein; APP; therapy;
KW Alzheimer's disease; antialzheimer's; aspartyl protease 1; Aspl;
KW beta-secretase.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Cleavage-site 4..5
XX
PN WO200123533-A2.
XX
PD 05-APR-2001.
XX
PF 22-SEP-2000; 2000WO-US26080.
XX
PR 23-SEP-1999; 99US-0155493.
PR 23-SEP-1999; 99WO-US20881.
PR 13-OCT-1999; 99US-0416901.
PR 06-DEC-1999; 99US-0169232.
XX
PA (PHAA ) PHARMACIA & UPJOHN CO.
XX
PI Gurney M, Bienkowski MJ;
XX
DR WPI; 2001-290516/30.
XX
PT Enzymes that cleave the alpha-secretase site of the amyloid precursor
PT protein, useful for the treatment of Alzheimer's disease -
XX
PS Example 15; Page 94; 189pp; English.
XX
CC The present invention relates to enzymes for cleaving the alpha-
CC secretase site of the amyloid precursor protein (APP) and methods of
CC identifying those enzymes. The methods may be used to identify enzymes
CC that may be used to cleave the alpha-secretase cleavage site of the APP
CC protein. The enzymes may be used to treat or modulate the progress of
CC Alzheimer's disease. The present sequence is human Aspartyl protease-1
CC (hu-Asp-1) beta-secretase, wild-type peptide which is used for
CC determining the enzymatic activity of Asp-1 deltaTM (His)6 protein.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
   |||||
Db 1 EVKMDAEF 8

```

RESULT 8

ABB78621

ID ABB78621 standard; Peptide; 8 AA.

XX

AC ABB78621;

XX

DT 16-JUL-2002 (first entry)

XX

DE APP Swedish mutant form beta-secretase processing site SEQ ID NO:70.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease;

KW proteolytic.

XX

OS Synthetic.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-0025934.

XX

PR 23-SEP-1999; 99US-155493P.

PR 23-SEP-1999; 99US-0404133.

PR 23-SEP-1999; 99WO-US20881.

PR 13-OCT-1999; 99US-0416901.

PR 06-DEC-1999; 99US-169232P.

PR 22-SEP-2000; 2000GB-0023315.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-396337/43.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect

PT aspartyl protease activity, e.g. for the diagnosis of Alzheimer's

PT disease -

XX

PS Example 12; Page 85; 182pp; English.

XX

CC The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC substrate (I) which comprises a peptide of no more than 50 amino acids,
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC nucleotide sequence that hybridises under stringent conditions to the
CC non-coding strand complementary to a defined 1804 nucleotide sequence
CC (see ABL52456) where the nucleotide sequence encodes a polypeptide having
CC Asp1 proteolytic activity and lacks nucleotides encoding a transmembrane
CC domain); (3) a purified polynucleotide (III') comprising a sequence that
CC hybridises under stringent conditions to (III) (the nucleotide sequence
CC encodes a polypeptide further lacking a pro-peptide domain corresponding
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC comprising (III) or (III'); and (5) a host cell (V) transformed or
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC substrate (I) may be used as an enzyme substrate in assays to detect

CC aspartyl protease activity, (II) and therefore diagnose diseases
CC associated with aberrant hu-Asp1 expression and activity such as
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC sequence represents the amino acid sequence of a peptide that includes
CC the beta-secretase processing site within the Swedish mutant form of
CC amyloid precursor protein (APP), which is used in an example from the
CC present invention.

XX

SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 23; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 1 EVKMDAEF 8

RESULT 9

AAW82083

ID AAW82083 standard; peptide; 9 AA.

XX

AC AAW82083;

XX

DT 18-FEB-1999 (first entry)

XX

DE Fluorogenic protease indicator protease binding peptide #61.

XX

KW Protease activity; fluorophore; detection; fluorogenic; cellular uptake;
KW conformation change.

XX

OS Synthetic.

XX

PN WO9837226-A1.

XX

PD 27-AUG-1998.

XX

PF 20-FEB-1998; 98WO-US03000.

XX

PR 20-FEB-1997; 97US-0802981.

XX

PA (ONCO-) ONCOIMMUNIN INC.

XX

PI Komoriya A, Packard BS;

XX

DR WPI; 1998-467579/40.

XX

PT New fluorogenic compositions - containing 2 fluorophores separated
PT by a peptide comprising a protease binding site, used for detecting
PT protease activity in samples.

XX

PS Claim 4; Page 77; 90pp; English.

XX

CC AAW82023-W82240 are peptides used in the construction of a fluorogenic
CC composition which is used for the detection of protease activity in

CC biological samples. The products can be used for the detection of
 CC conformation changes in nucleic acids, oligosaccharides,
 CC polysaccharides, proteins, peptides, lipids, phospholipids, glycolipids,
 CC glycoproteins, steroids or polymers. In addition, attachment of a
 CC hydrophobic group to a molecule can be used to enhance uptake by cells.
 CC The composition is composed of P = peptide comprising a protease binding
 CC site for the protease, F1, F2 peptides = fluorophores where F1 is
 CC attached to the amino terminal amino acid and F2 is attached to the
 CC carboxyl terminal amino acid and S1, S2 peptides = when present, are
 CC peptide spacers where S1, when present, is attached to the amino terminal
 CC acid, and S2, when present, is attached to the carboxyl terminal amino
 CC acid.

XX

SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 19; Length 9;
 Best Local Similarity 100.0%; Pred. No. 9.3e+05;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 EVKMDAEF 8
 |||||
 Db 2 EVKMDAEF 9

RESULT 10

AAB07873

ID AAB07873 standard; peptide; 9 AA.

XX

AC AAB07873;

XX

DT 14-NOV-2000 (first entry)

XX

DE A peptide fragment derived from beta-amyloid precursor protein.

XX

KW Beta-secretase; beta-amyloid precursor protein; beta-amyloid peptide;
 KW amyloid plaque component; Alzheimer's disease; amyloidogenic disease;
 KW inhibitor.

XX

OS Homo sapiens.

XX

PN WO200047618-A2.

XX

PD 17-AUG-2000.

XX

PF 10-FEB-2000; 2000WO-US03819.

XX

PR 10-FEB-1999; 99US-0119571.

PR 15-JUN-1999; 99US-0139172.

XX

PA (ELAN-) ELAN PHARM INC.

XX

PI Anderson JP, Basi G, Doane MT, Frigon N, John V, Power M;

PI Sinha S, Tatsuno G, Tung J, Wang S, McConlogue L;

XX

DR WPI; 2000-533011/48.

XX

PT Purified beta-secretase protein used in assays to discover inhibitors

PT which can be used for the treatment of amyloidogenic diseases e.g.
PT Alzheimer's disease -
XX
PS Disclosure; Page 12; 121pp; English.
XX
CC The specification describes a beta-secretase enzyme. The enzyme cleaves
CC beta-amyloid precursor protein to produce beta-amyloid peptide. This
CC enzyme is therefore implicated in the production of amyloid plaque
CC components which accumulate in the brains of individuals afflicted with
CC Alzheimer's disease. Inhibitors of beta-secretase are administered to
CC a mammalian subject e.g. with Alzheimer's disease or Alzheimer's
CC disease-like pathology to test if they maintain or improve cognitive
CC ability or reduce the plaque burden. The compounds are used for the
CC treatment of amyloidogenic diseases e.g. Alzheimer's disease. The
CC present sequence represents a peptide derived from beta-amyloid
CC precursor protein
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 21; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 11

AAAY87949

ID AAY87949 standard; protein; 9 AA.

XX

AC AAY87949;

XX

DT 11-SEP-2000 (first entry)

XX

DE Mammalian amyloid precursor protein substrate peptide.

XX

KW Amyloid precursor protein; APP; secretase; vesicle; Abeta peptide;

KW Alzheimer's disease.

XX

OS Mammalia.

XX

PN WO200023576-A2.

XX

PD 27-APR-2000.

XX

PF 15-OCT-1999; 99WO-US24403.

XX

PR 16-OCT-1998; 98US-0173887.

PR 20-APR-1999; 99US-0294987.

XX

PA (HOOK/) HOOK V Y H.

XX

PI Hook VYH;

XX

DR WPI; 2000-339679/29.

XX
PT Determining the proteolytic activity of secretase for treating
PT Alzheimer's disease comprises permeablizing vesicles and incubating
PT with amyloid precursor protein (APP) to determine cleavage of APP
PT substrate -
XX
PS Example XV; Page 97; 97pp; English.
XX
CC This invention describes a novel method for the determination of
CC the proteolytic activity of a secretase comprising obtaining and
CC permeablizing pure vesicles, incubating the vesicles with an amyloid
CC precursor protein (APP) and determining the cleavage of the APP
CC substrate where the amount of cleavage is proportional to the
CC proteolytic activity of the secretase. The methods are useful for
CC selecting secretases and agents that cleave the amyloid precursor
CC protein substrate, inhibiting production of the Abeta peptide found
CC in Alzheimer's disease and treating Alzheimer's disease in patients.
CC This sequence represents a mammalian amyloid precursor protein, APP
CC substrate which is used in the method of the invention.
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 21; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 12
ABU60430
ID ABU60430 standard; Peptide; 9 AA.
XX
AC ABU60430;
XX
DT 29-APR-2003 (first entry)
XX
DE Protease binding peptide motif SEQ ID 142.
XX
KW Protease; indicator; chromophore; H-dimer; fluorescence; absorbance;
KW nuclease; screening; fluorophore; substrate cleavage.
XX
OS Synthetic.
XX
PN WO200261038-A2.
XX
PD 08-AUG-2002.
XX
PF 21-DEC-2001; 2001WO-US49781.
XX
PR 22-DEC-2000; 2000US-0747287.
XX
PA (ONCO-) ONCOIMMUNIN INC.
XX
PI Packard BS, Komoriya A;

XX
DR WPI; 2002-698548/75.
XX
PT Indicator composition comprising polypeptide or nucleic acid backbone
PT joining two same chromophores resulting in quenching of fluorescence
PT of/change in absorbance of chromophores, useful for detecting protease
PT activity -
XX
PS Disclosure; Page 34; 97pp; English.
XX
CC This invention describes a novel indicator composition (referred as
CC homo-doubly labeled compositions) comprising a polypeptide backbone or
CC a nucleic acid backbone joining two chromophores of the same species
CC whereby the chromophores form an H-dimer resulting in quenching of the
CC fluorescence of or a change in the absorbance of the chromophore, a
CC decrease in fluorescence or a change in absorbance indicates that the
CC first molecule and the second molecule are interacting. The indicator is
CC useful for detecting the activity of a protease, where an increase in
CC fluorescence or a change in absorbance indicates that the protease
CC cleaves the polypeptide backbone. The indicator is attached to a solid
CC support inside a mammalian, yeast or insect cell. The composition bears a
CC hydrophobic group such as Fmoc, 9-fluoreneacetyl group,
CC 1-fluorene-carboxylic group, 9-fluorene-carboxylic group, and
CC 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl
CC (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,
CC 6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts),
CC 4,4'-dimethoxybenzhydryl (Mbh), etc. The method described in the
CC invention is useful for detecting protease or nuclease activity (or the
CC presence of nucleic acid) in histological section, cells in culture,
CC (e.g., seeded or cultured adherent cells), a biological sample such as
CC tissue, biopsy, lymph, embryo, or whole animal, or cell suspension
CC derived from a biological sample such as tissue, blood, urine, saliva,
CC lymph, or biopsy. The indicator composition is also useful for screening
CC a test agent for the ability to modulate a protease (or a nuclease,
CC lipase, etc.). The indicator reagents allow rapid determination of
CC protease activity in a matter of minutes in a single-step procedure. The
CC fluorescent indicators both absorb and emit in the visible range (400-800
CC nm). These signals are therefore not readily quenched by, nor is
CC activation of the fluorophores, that is, absorption of light, interfered
CC with by background molecules; therefore they are easily detected in
CC biological samples. The fluorogenic protease indicators utilise high
CC efficiency fluorophores and are able to achieve a high degree of
CC quenching while providing a strong signal when the quench is released by
CC cleavage of the peptide substrate. The high signal allows detection of
CC very low levels of protease activity. Thus the fluorogenic protease
CC indicators are particularly well suited for in situ detection of protease
CC activity. ABU60357-ABU60477 represent peptides used to illustrate the
CC method described in the disclosure of the invention.
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 23; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |

Db

2 EVKMDAEF 9

RESULT 13

AAR22054

ID AAR22054 standard; peptide; 10 AA.

XX

AC AAR22054;

XX

DT 25-MAR-2003 (updated)

DT 06-JUL-1992 (first entry)

XX

DE Peptide P1.

XX

KW Beta amyloid; protein precursor; protease; Alzheimers disease;
KW radioiodination;

XX

OS Synthetic.

XX

FH Key Location/Qualifiers

FT Modified-site 1

FT /note= "site of radioiodination"

XX

PN WO9203542-A.

XX

PD 05-MAR-1992.

XX

PF 19-AUG-1991; 91WO-UO05932.

XX

PR 17-AUG-1990; 90US-0568806.

XX

PA (UYBO-) UNIV BOSTON.

XX

PI Abraham CR;

XX

DR WPI; 1992-096886/12.

XX

PT Treatment and diagnosis of Alzheimer's disease - by reducing
PT beta-protein precursor proteolysis near beta-protein N-terminus
PT by administering proteolysis inhibitor

XX

PS Disclosure; Page 6; 29pp; English.

XX

CC The synthetic peptide substrate P1 was used to assay for proteases
CC that cleave in the vicinity of the N-terminus of the amyloid beta
CC protein. The peptide corresponds to the beta protein precursor
CC sequence flanking that site. The peptide starts five amino acids
CC upstream from the N-terminus (at Asp) of the beta protein, and
CC extends across the putative cleavage site into the beta protein
CC itself. Histidine was substituted for the native isoleucine to give
CC a site for radioiodination. Labelled peptide was incubated with
CC brain fractions from Alzheimers disease patients. The resulting
CC fragments were separated by TLC and N-terminal fragments detected by
CC autoradiography.

CC See also AAR22055,6.

CC (Updated on 25-MAR-2003 to correct PA field.)

XX

SQ Sequence 10 AA;

Query Match 100.0%; Score 40; DB 13; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.024;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 3 EVKMDAEF 10

RESULT 14

AAR24261

ID AAR24261 standard; Protein; 10 AA.

XX

AC AAR24261;

XX

DT 25-MAR-2003 (updated)

DT 09-NOV-1992 (first entry)

XX

DE Human amyloidin protease substrate sequence #1.

XX

KW Alzheimer's disease; beta amyloid precursor protein; APP; zinc;

KW metalloprotease; hAP; protease inhibitor; APP592-601

XX

OS Synthetic.

XX

FH Key Location/Qualifiers

FT Modified-site 1

FT /note= "Acetylated-Ser"

XX

PN W09207068-A1.

XX

PD 30-APR-1992.

XX

PF 04-OCT-1991; 91WO-US07290.

XX

PR 05-OCT-1990; 90US-0594122.

PR 30-SEP-1991; 91US-0766351.

XX

PA (ATHE-) ATHENA NEUROSCIENCES INC.

PA (ELIL) LILLY & CO ELI.

XX

PI Dovey HF, Johnstone EM, Little SP, McConlogue L, Seubert PA;

PI Sinha S;

XX

DR WPI; 1992-167148/20.

XX

PT Human amyloidin protease - used for cleaving Met-Asp bond in

PT amyloid-like substrate for identifying protease inhibitors

XX

PS Claim 1; Page 52; 62pp; English.

XX

CC Claimed human amyloidin protease is defined by its ability to

CC cleave the Met-Asp bond of this synthetic substrate. The substrate,

CC which corresponds to residues 592 to 601 of the 695 amino acid APP,

CC can be used in an assay for identifying inhibitors of proteases

CC which cleave Met-Asp bonds, e.g. amyloidin, human skin chymase or
CC rat mast cell protease I or II.
CC See AAR24260-3, AAR24266-7 and AAQ24875-Q24887.
CC (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ Sequence 10 AA;

Query Match 100.0%; Score 40; DB 13; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.024;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 15

AAW82440

ID AAW82440 standard; peptide; 10 AA.

XX

AC AAW82440;

XX

DT 24-FEB-1999 (first entry)

XX

DE Human amyloid beta-protein N-terminal domain peptide P1.

XX

KW Amyloid beta-protein precursor; endoprotease; human; brain; screening;

KW Alzheimer's disease; O-phenanthroline; metal chelator; treatment;

KW pheymethylsulphonyl fluoride; protease inhibitor.

XX

OS Homo sapiens.

XX

PN US5849560-A.

XX

PD 15-DEC-1998.

XX

PF 26-FEB-1993; 93US-0025321.

XX

PR 26-FEB-1993; 93US-0025321.

PR 17-AUG-1990; 90US-0568806.

PR 05-APR-1991; 91US-0681093.

XX

PA (UYBO-) UNIV BOSTON.

XX

PI Abraham CR;

XX

DR WPI; 1999-069739/06.

XX

PT Purified endoprotease associated with Alzheimer's disease - is
PT prepared from fractions of brain tissue homogenate and is useful for
PT drug screening

XX

PS Claim 1; Column 17-18; 27pp; English.

XX

CC This sequence is the N-terminal domain of the amyloid beta-protein
CC precursor which is cleaved by a purified endoprotease from human brain
CC tissue homogenate and is identical to an endoprotease found in the

CC brains of humans with Alzheimer's disease. The endoprotease is inhibited
CC by O-phenanthroline and by metal chelators and is not inhibited by
CC pheymethylsulphonyl fluoride. The endoprotease is useful to screen for
CC protease inhibitors that might be useful for treating Alzheimer's disease
CC by inhibiting cleavage of the N-terminal domain of amyloid beta -protein
CC precursor.

XX

SQ Sequence 10 AA;

Query Match 100.0%; Score 40; DB 20; Length 10;

Best Local Similarity 100.0%; Pred. No. 0.024;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8

|||||||

Db 3 EVKMDAEF 10

Search completed: January 21, 2004, 09:22:26

Job time : 2.1109 secs

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OM protein - protein search, using sw model

Run on: January 21, 2004, 09:19:55 ; Search time 0.718929 Seconds
 (without alignments)
 470.821 Million cell updates/sec

Title: US-09-869-414A-67
 Perfect score: 40
 Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
 Gapop 10.0 , Gapext 0.5

Searched: 328717 seqs, 42310858 residues

Total number of hits satisfying chosen parameters: 328717

Minimum DB seq length: 0
 Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
 Maximum Match 100%
 Listing first 45 summaries

Database : Issued Patents AA:*
 1: /cgn2_6/ptodata/1/iaa/5A_COMB.pep:*
 2: /cgn2_6/ptodata/1/iaa/5B_COMB.pep:*
 3: /cgn2_6/ptodata/1/iaa/6A_COMB.pep:*
 4: /cgn2_6/ptodata/1/iaa/6B_COMB.pep:*
 5: /cgn2_6/ptodata/1/iaa/PCTUS_COMB.pep:*
 6: /cgn2_6/ptodata/1/iaa/backfiles1.pep:*

Pred. No. is the number of results predicted by chance to have a
 score greater than or equal to the score of the result being printed,
 and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | % | | DB | ID | Description |
|---------------|-------|-------|--------------|----|-------------------|-------------------|
| | | Query | Match Length | | | |
| 1 | 40 | 100.0 | 8 | 4 | US-09-548-372D-67 | Sequence 67, Appl |
| 2 | 40 | 100.0 | 8 | 4 | US-09-548-367D-67 | Sequence 67, Appl |
| 3 | 40 | 100.0 | 8 | 4 | US-09-551-853D-67 | Sequence 67, Appl |
| 4 | 40 | 100.0 | 9 | 3 | US-08-802-981-221 | Sequence 221, App |
| 5 | 40 | 100.0 | 9 | 4 | US-09-294-987-6 | Sequence 6, Appli |
| 6 | 40 | 100.0 | 10 | 2 | US-08-025-321C-1 | Sequence 1, Appli |
| 7 | 40 | 100.0 | 10 | 4 | US-09-548-372D-64 | Sequence 64, Appl |
| 8 | 40 | 100.0 | 10 | 4 | US-09-548-367D-64 | Sequence 64, Appl |
| 9 | 40 | 100.0 | 10 | 4 | US-09-551-853D-64 | Sequence 64, Appl |
| 10 | 40 | 100.0 | 10 | 4 | US-09-604-608-4 | Sequence 4, Appli |
| 11 | 40 | 100.0 | 11 | 5 | PCT-US94-07043A-7 | Sequence 7, Appli |

| | | | | | | |
|----|----|-------|-----|---|-------------------|-------------------|
| 12 | 40 | 100.0 | 12 | 5 | PCT-US94-07043A-2 | Sequence 2, Appli |
| 13 | 40 | 100.0 | 15 | 4 | US-09-548-372D-71 | Sequence 71, Appl |
| 14 | 40 | 100.0 | 15 | 4 | US-09-548-367D-71 | Sequence 71, Appl |
| 15 | 40 | 100.0 | 15 | 4 | US-09-551-853D-71 | Sequence 71, Appl |
| 16 | 40 | 100.0 | 16 | 5 | PCT-US94-07043A-1 | Sequence 1, Appli |
| 17 | 40 | 100.0 | 21 | 3 | US-08-802-981-114 | Sequence 114, App |
| 18 | 40 | 100.0 | 27 | 1 | US-08-141-324-11 | Sequence 11, Appl |
| 19 | 40 | 100.0 | 27 | 1 | US-08-541-902-11 | Sequence 11, Appl |
| 20 | 40 | 100.0 | 45 | 1 | US-08-462-859A-5 | Sequence 5, Appli |
| 21 | 40 | 100.0 | 45 | 1 | US-08-123-659A-5 | Sequence 5, Appli |
| 22 | 40 | 100.0 | 45 | 1 | US-08-464-247A-5 | Sequence 5, Appli |
| 23 | 40 | 100.0 | 45 | 1 | US-08-464-248A-5 | Sequence 5, Appli |
| 24 | 40 | 100.0 | 58 | 1 | US-08-371-930-25 | Sequence 25, Appl |
| 25 | 40 | 100.0 | 58 | 5 | PCT-US94-01712-25 | Sequence 25, Appl |
| 26 | 40 | 100.0 | 59 | 1 | US-08-484-969-3 | Sequence 3, Appli |
| 27 | 40 | 100.0 | 59 | 1 | US-08-472-627-3 | Sequence 3, Appli |
| 28 | 40 | 100.0 | 59 | 1 | US-08-388-463-3 | Sequence 3, Appli |
| 29 | 40 | 100.0 | 63 | 1 | US-08-462-859A-3 | Sequence 3, Appli |
| 30 | 40 | 100.0 | 63 | 1 | US-08-462-859A-4 | Sequence 4, Appli |
| 31 | 40 | 100.0 | 63 | 1 | US-08-123-659A-3 | Sequence 3, Appli |
| 32 | 40 | 100.0 | 63 | 1 | US-08-123-659A-4 | Sequence 4, Appli |
| 33 | 40 | 100.0 | 63 | 1 | US-08-464-247A-3 | Sequence 3, Appli |
| 34 | 40 | 100.0 | 63 | 1 | US-08-464-247A-4 | Sequence 4, Appli |
| 35 | 40 | 100.0 | 63 | 1 | US-08-464-248A-3 | Sequence 3, Appli |
| 36 | 40 | 100.0 | 63 | 1 | US-08-464-248A-4 | Sequence 4, Appli |
| 37 | 40 | 100.0 | 103 | 2 | US-08-404-831-2 | Sequence 2, Appli |
| 38 | 40 | 100.0 | 103 | 2 | US-08-612-785B-2 | Sequence 2, Appli |
| 39 | 40 | 100.0 | 103 | 2 | US-08-475-579A-2 | Sequence 2, Appli |
| 40 | 40 | 100.0 | 103 | 2 | US-08-920-162A-2 | Sequence 2, Appli |
| 41 | 40 | 100.0 | 103 | 3 | US-08-339-708A-10 | Sequence 10, Appl |
| 42 | 40 | 100.0 | 103 | 3 | US-09-356-931-2 | Sequence 2, Appli |
| 43 | 40 | 100.0 | 103 | 4 | US-08-703-675C-2 | Sequence 2, Appli |
| 44 | 40 | 100.0 | 103 | 4 | US-08-617-267C-2 | Sequence 2, Appli |
| 45 | 40 | 100.0 | 105 | 2 | US-08-729-345-1 | Sequence 1, Appli |

ALIGNMENTS

RESULT 1
 US-09-548-372D-67
 ; Sequence 67, Application US/09548372D
 ; Patent No. 6420534
 ; GENERAL INFORMATION:
 ; APPLICANT: GURNEY ET AL.
 ; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
 AND USES
 ; TITLE OF INVENTION: THEREOF
 ; FILE REFERENCE: 29915/6280I
 ; CURRENT APPLICATION NUMBER: US/09/548,372D
 ; CURRENT FILING DATE: 2000-04-12
 ; PRIOR APPLICATION NUMBER: US 60/155,493
 ; PRIOR FILING DATE: 1999-09-23
 ; PRIOR APPLICATION NUMBER: US 09/404,133
 ; PRIOR FILING DATE: 1999-09-23
 ; PRIOR APPLICATION NUMBER: PCT/US99/20881
 ; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Peptide
US-09-548-372D-67

Query Match 100.0%; Score 40; DB 4; Length 8;
Best Local Similarity 100.0%; Pred. No. 2.5e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 1 EVKMDAEF 8

RESULT 2

US-09-548-367D-67

; Sequence 67, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Peptide
US-09-548-367D-67

Query Match 100.0%; Score 40; DB 4; Length 8;
Best Local Similarity 100.0%; Pred. No. 2.5e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |

Db 1 EVKMDAEF 8

RESULT 3

US-09-551-853D-67

; Sequence 67, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280L
; CURRENT APPLICATION NUMBER: US/09/551,853D
; CURRENT FILING DATE: 2000-04-18
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Peptide
US-09-551-853D-67

Query Match 100.0%; Score 40; DB 4; Length 8;
Best Local Similarity 100.0%; Pred. No. 2.5e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 EVKMDAEF 8
|||
Db 1 EVKMDAEF 8

RESULT 4

US-08-802-981-221

; Sequence 221, Application US/08802981
; Patent No. 6037137
; GENERAL INFORMATION:
; APPLICANT: Komoriya, Akira
; APPLICANT: Packard, Beverly S.
; TITLE OF INVENTION: Compositions for the Detection of Enzyme
; TITLE OF INVENTION: Activity in Biological Samples and Methods of Use
Thereof
; NUMBER OF SEQUENCES: 231
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Townsend and Townsend and Crew LLP
; STREET: Two Embarcadero Center, Eighth Floor
; CITY: San Francisco

```

; STATE: California
; COUNTRY: USA
; ZIP: 94111-3834
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/802,981
; FILING DATE: 20-FEB-1997
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Hunter, Tom
; REGISTRATION NUMBER: 38,498
; REFERENCE/DOCKET NUMBER: 016865-000300US
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (415) 576-0200
; TELEFAX: (415) 576-0300
; INFORMATION FOR SEQ ID NO: 221:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 9 amino acids
; TYPE: amino acid
; STRANDEDNESS:
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
US-08-802-981-221

```

```

Query Match          100.0%; Score 40; DB 3; Length 9;
Best Local Similarity 100.0%; Pred. No. 2.5e+05;
Matches      8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy      1 EVKMDAEF 8
        |||||
Db      2 EVKMDAEF 9

```

```

RESULT 5
US-09-294-987-6
; Sequence 6, Application US/09294987
; Patent No. 6313268
; GENERAL INFORMATION:
; APPLICANT: Hook, Vivian Y.H.
; TITLE OF INVENTION: SECRETASES RELATED TO ALZHEIMER'S DEMENTIA
; FILE REFERENCE: P-AS 3515
; CURRENT APPLICATION NUMBER: US/09/294,987
; CURRENT FILING DATE: 1999-04-20
; PRIOR APPLICATION NUMBER: US 09/173,887
; PRIOR FILING DATE: 1998-10-16
; NUMBER OF SEQ ID NOS: 6
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 6
; LENGTH: 9
; TYPE: PRT
; ORGANISM: mammalian
US-09-294-987-6

```

Query Match 100.0%; Score 40; DB 4; Length 9;
Best Local Similarity 100.0%; Pred. No. 2.5e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 6

US-08-025-321C-1

; Sequence 1, Application US/08025321C
; Patent No. 5849560

; GENERAL INFORMATION:

; APPLICANT: Abraham Ph.D., Carmela R.
; TITLE OF INVENTION: PROTEASES CAUSING ABNORMAL DEGREDEATION
; TITLE OF INVENTION: OF AMYLOID BETA-PROTEIN PRECURSOR
; NUMBER OF SEQUENCES: 13

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Choate, Hall & Stewart
; STREET: 53 State Street
; CITY: Boston
; STATE: MA
; COUNTRY: USA
; ZIP: 02109

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/025,321C
; FILING DATE: 26-FEB-1993
; CLASSIFICATION: 435

; ATTORNEY/AGENT INFORMATION:

; NAME: Jarrell Ph.D., Brenda H.
; REGISTRATION NUMBER: 39,223
; REFERENCE/DOCKET NUMBER: 0079571-0034

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: 617 248 5000
; TELEFAX: 617 248 4000

; INFORMATION FOR SEQ ID NO: 1:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 10 amino acids
; TYPE: amino acid
; STRANDEDNESS: not relevant
; TOPOLOGY: not relevant
; MOLECULE TYPE: peptide

US-08-025-321C-1

Query Match 100.0%; Score 40; DB 2; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.015;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 3 EVKMDAEF 10

RESULT 7

US-09-548-372D-64

; Sequence 64, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 64

; LENGTH: 10

; TYPE: PRT

; ORGANISM: Artificial sequence

; FEATURE:

; OTHER INFORMATION: Synthetic peptide

US-09-548-372D-64

Query Match 100.0%; Score 40; DB 4; Length 10;

Best Local Similarity 100.0%; Pred. No. 0.015;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8

|||||||

Db 2 EVKMDAEF 9

RESULT 8

US-09-548-367D-64

; Sequence 64, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Synthetic peptide
US-09-548-367D-64

Query Match 100.0%; Score 40; DB 4; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.015;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 9

US-09-551-853D-64

; Sequence 64, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280L
; CURRENT APPLICATION NUMBER: US/09/551,853D
; CURRENT FILING DATE: 2000-04-18
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Synthetic peptide
US-09-551-853D-64

Query Match 100.0%; Score 40; DB 4; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.015;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 10

US-09-604-608-4

; Sequence 4, Application US/09604608
; Patent No. 6545127
; GENERAL INFORMATION:
; APPLICANT: Tang, Jordan J.N.
; APPLICANT: Lin, Xinli
; APPLICANT: Koelsch, Gerald
; TITLE OF INVENTION: Catalytically Active Recombinant Memapsin and Methods
; TITLE OF INVENTION: of Use Thereof
; FILE REFERENCE: OMRF 179
; CURRENT APPLICATION NUMBER: US/09/604,608
; CURRENT FILING DATE: 2000-06-27
; PRIOR APPLICATION NUMBER: 60/141,363
; PRIOR FILING DATE: 1999-06-28
; PRIOR APPLICATION NUMBER: 60/168,060
; PRIOR FILING DATE: 1999-11-30
; PRIOR APPLICATION NUMBER: 60/177,836
; PRIOR FILING DATE: 2000-01-25
; PRIOR APPLICATION NUMBER: 60/178,368
; PRIOR FILING DATE: 2000-01-27
; PRIOR APPLICATION NUMBER: 60/210,292
; PRIOR FILING DATE: 2000-06-08
; NUMBER OF SEQ ID NOS: 31
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-604-608-4

Query Match 100.0%; Score 40; DB 4; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.015;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 11

PCT-US94-07043A-7

; Sequence 7, Application PC/TUS9407043A
; GENERAL INFORMATION:
; APPLICANT: Tamburini, Paul P.; Benz, G nter; H bich,
; APPLICANT: Dieter; Dreyer, Robert N.; Koenig, Gerhard
; TITLE OF INVENTION: CATHEPSIN D IS AN AMYLOIDOGENIC
; TITLE OF INVENTION: PROTEASE IN ALZHEIMER S DISEASE
; NUMBER OF SEQUENCES: 11
; CORRESPONDENCE ADDRESS:

```

; ADDRESSEE: Miles Inc.
; STREET: 400 Morgan Lane
; CITY: West Haven
; STATE: Connecticut
; COUNTRY: USA
; ZIP: 06516
;
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette, 3.50 inch, 800 kb storage
; COMPUTER: Sharp PC 4600
; OPERATING SYSTEM: MS-DOS
; SOFTWARE: WordPerfect 5.1
;
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: PCT/US94/07043A
; FILING DATE: June 21, 1994
; CLASSIFICATION:
;
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/US93/10889
; FILING DATE: November 12, 1993
;
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/995,660
; FILING DATE: December 16, 1992
;
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/880,914
; FILING DATE: May 11, 1992
;
; ATTORNEY/AGENT INFORMATION:
; NAME: Pamela A. Simonton
; REGISTRATION NUMBER: 31,060
; REFERENCE/DOCKET NUMBER: MTI 224.3
;
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (203) 937-2340
; TELEFAX: (203) 937-2795
;
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 11 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
PCT-US94-07043A-7

```

```

Query Match          100.0%; Score 40; DB 5; Length 11;
Best Local Similarity 100.0%; Pred. No. 0.016;
Matches      8; Conservative    0; Mismatches    0; Indels      0; Gaps      0;

```

```

Qy      1 EVKMDAEF 8
        |||||
Db      3 EVKMDAEF 10

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RESULT 12

PCT-US94-07043A-2

; Sequence 2, Application PC/TUS9407043A

; GENERAL INFORMATION:

```

; APPLICANT: Tamburini, Paul P.; Benz, G nter; H bich,
; APPLICANT: Dieter; Dreyer, Robert N.; Koenig, Gerhard
; TITLE OF INVENTION: CATHEPSIN D IS AN AMYLOIDOGENIC
; TITLE OF INVENTION: PROTEASE IN ALZHEIMER S DISEASE
; NUMBER OF SEQUENCES: 11
; CORRESPONDENCE ADDRESS:

```

```

; ADDRESSEE: Miles Inc.
; STREET: 400 Morgan Lane
; CITY: West Haven
; STATE: Connecticut
; COUNTRY: USA
; ZIP: 06516
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette, 3.50 inch, 800 kb storage
; COMPUTER: Sharp PC 4600
; OPERATING SYSTEM: MS-DOS
; SOFTWARE: WordPerfect 5.1
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: PCT/US94/07043A
; FILING DATE: June 21, 1994
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/US93/10889
; FILING DATE: November 12, 1993
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/995,660
; FILING DATE: December 16, 1992
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/880,914
; FILING DATE: May 11, 1992
; ATTORNEY/AGENT INFORMATION:
; NAME: Pamela A. Simonton
; REGISTRATION NUMBER: 31,060
; REFERENCE/DOCKET NUMBER: MTI 224.3
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (203) 937-2340
; TELEFAX: (203) 937-2795
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 12 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
PCT-US94-07043A-2

```

```

Query Match          100.0%; Score 40; DB 5; Length 12;
Best Local Similarity 100.0%; Pred. No. 0.018;
Matches      8; Conservative    0; Mismatches    0; Indels      0; Gaps      0;

```

```

Qy      1 EVKMDAEF 8
        |||||
Db      3 EVKMDAEF 10

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RESULT 13
US-09-548-372D-71
; Sequence 71, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I

```


; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 71
; LENGTH: 15
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: peptide
US-09-548-372D-71

Query Match 100.0%; Score 40; DB 4; Length 15;
Best Local Similarity 100.0%; Pred. No. 0.022;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 4 EVKMDAEF 11

RESULT 14
US-09-548-367D-71
; Sequence 71, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 71
; LENGTH: 15
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: peptide

US-09-548-367D-71

Query Match 100.0%; Score 40; DB 4; Length 15;
Best Local Similarity 100.0%; Pred. No. 0.022;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 4 EVKMDAEF 11

RESULT 15

US-09-551-853D-71

; Sequence 71, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280L
; CURRENT APPLICATION NUMBER: US/09/551,853D
; CURRENT FILING DATE: 2000-04-18
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 71
; LENGTH: 15
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: peptide
US-09-551-853D-71

Query Match 100.0%; Score 40; DB 4; Length 15;
Best Local Similarity 100.0%; Pred. No. 0.022;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 4 EVKMDAEF 11

Search completed: January 21, 2004, 09:27:08
Job time : 0.718929 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:16:55 ; Search time 0.734226 Seconds
(without alignments)
1047.838 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283308 seqs, 96168682 residues

Total number of hits satisfying chosen parameters: 283308

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR_76:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,
and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query | | DB | ID | Description |
|---------------|-------|-------|--------|----|--------|--------------------|
| | | Match | Length | | | |
| 1 | 40 | 100.0 | 33 | 2 | S23094 | beta-amyloid prote |
| 2 | 40 | 100.0 | 57 | 2 | E60045 | Alzheimer's diseas |
| 3 | 40 | 100.0 | 57 | 2 | F60045 | Alzheimer's diseas |
| 4 | 40 | 100.0 | 57 | 2 | G60045 | Alzheimer's diseas |
| 5 | 40 | 100.0 | 57 | 2 | D60045 | Alzheimer's diseas |
| 6 | 40 | 100.0 | 57 | 2 | A60045 | Alzheimer's diseas |
| 7 | 40 | 100.0 | 57 | 2 | B60045 | Alzheimer's diseas |
| 8 | 40 | 100.0 | 82 | 2 | PQ0438 | Alzheimer's diseas |
| 9 | 40 | 100.0 | 695 | 1 | A49795 | Alzheimer's diseas |
| 10 | 40 | 100.0 | 695 | 2 | A27485 | Alzheimer's diseas |
| 11 | 40 | 100.0 | 695 | 2 | S00550 | Alzheimer's diseas |
| 12 | 40 | 100.0 | 770 | 1 | QRHUA4 | Alzheimer's diseas |
| 13 | 34 | 85.0 | 142 | 2 | E89026 | protein F13A2.1 [i |

| | | | | | | |
|----|----|------|------|---|--------|----------------------|
| 14 | 34 | 85.0 | 747 | 2 | JH0773 | Alzheimer's diseases |
| 15 | 33 | 82.5 | 626 | 2 | AF0358 | conserved hypothet |
| 16 | 32 | 80.0 | 354 | 2 | S51143 | FMO-protein - Chlo |
| 17 | 32 | 80.0 | 426 | 2 | G75187 | probable trehalose |
| 18 | 32 | 80.0 | 929 | 2 | T52517 | hypothetical prote |
| 19 | 32 | 80.0 | 1906 | 2 | AD2443 | hypothetical prote |
| 20 | 31 | 77.5 | 282 | 2 | T26112 | hypothetical prote |
| 21 | 31 | 77.5 | 3562 | 2 | A47171 | chondroitin sulfat |
| 22 | 30 | 75.0 | 233 | 2 | T03329 | probable amidase 1 |
| 23 | 30 | 75.0 | 375 | 2 | A83352 | probable glyceroph |
| 24 | 30 | 75.0 | 584 | 2 | A97171 | uncharacterized pr |
| 25 | 30 | 75.0 | 627 | 2 | AB0535 | hypothetical prote |
| 26 | 30 | 75.0 | 774 | 2 | AG1565 | autolysin (amidase |
| 27 | 30 | 75.0 | 793 | 2 | T27133 | hypothetical prote |
| 28 | 29 | 72.5 | 84 | 2 | T27174 | hypothetical prote |
| 29 | 29 | 72.5 | 182 | 2 | B97000 | hypothetical prote |
| 30 | 29 | 72.5 | 242 | 2 | C96606 | hypothetical prote |
| 31 | 29 | 72.5 | 280 | 2 | T09939 | hypothetical prote |
| 32 | 29 | 72.5 | 286 | 2 | G85230 | hypothetical prote |
| 33 | 29 | 72.5 | 385 | 2 | G97350 | xylR transcription |
| 34 | 29 | 72.5 | 400 | 2 | E69446 | hypothetical prote |
| 35 | 29 | 72.5 | 408 | 2 | F70369 | carboxyl-terminal |
| 36 | 29 | 72.5 | 452 | 2 | S56938 | fructose-2,6-bisph |
| 37 | 29 | 72.5 | 463 | 2 | T38111 | atrazine chlorohyd |
| 38 | 29 | 72.5 | 464 | 2 | T38356 | septin homolog spn |
| 39 | 29 | 72.5 | 470 | 2 | C75591 | threonine synthase |
| 40 | 29 | 72.5 | 491 | 2 | F64118 | cytosolic axial fi |
| 41 | 29 | 72.5 | 526 | 2 | D71805 | protein-export mem |
| 42 | 29 | 72.5 | 844 | 2 | T32608 | hypothetical prote |
| 43 | 29 | 72.5 | 871 | 2 | T43427 | pob1 protein - fis |
| 44 | 29 | 72.5 | 949 | 1 | S55478 | pyruvate, phosphat |
| 45 | 29 | 72.5 | 1378 | 2 | G88637 | protein F53H1.4 [i |

ALIGNMENTS

RESULT 1

S23094

beta-amyloid protein precursor - rat

C;Species: Rattus norvegicus (Norway rat)

C;Date: 22-Nov-1993 #sequence_revision 10-Nov-1995 #text_change 03-May-1996

C;Accession: S23094

R;Kojima, S.; Omori, M.

FEBS Lett. 304, 57-60, 1992

A;Title: Two-way cleavage of beta-amyloid protein precursor by multicatalytic proteinase.

A;Reference number: S23094; MUID:92316198; PMID:1618299

A;Accession: S23094

A;Molecule type: protein

A;Residues: 1-33 <KOJ>

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

Query Match 100.0%; Score 40; DB 2; Length 33;

Best Local Similarity 100.0%; Pred. No. 0.024;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 2 EVKMDAEF 9

RESULT 2

E60045

Alzheimer's disease amyloid beta/A4 protein precursor - sheep (fragment)

C;Species: Ovis sp. (sheep)

C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995

C;Accession: E60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: E60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56130

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 2 EVKMDAEF 9

RESULT 3

F60045

Alzheimer's disease amyloid beta/A4 protein precursor - pig (fragment)

C;Species: Sus scrofa domestica (domestic pig)

C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999

C;Accession: F60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: F60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56127; NID:g1895; PIDN:CAA39592.1; PID:g1896

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 0.044;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 2 EVKMDAEF 9

RESULT 4

G60045

Alzheimer's disease amyloid beta/A4 protein precursor - guinea pig (fragment)

C;Species: Cavia porcellus (guinea pig)

C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995

C;Accession: G60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: G60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56126

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;

Best Local Similarity 100.0%; Pred. No. 0.044;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 2 EVKMDAEF 9

RESULT 5

D60045

Alzheimer's disease amyloid beta/A4 protein precursor - bovine (fragment)

C;Species: Bos primigenius taurus (cattle)

C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995

C;Accession: D60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: D60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56124

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;

Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 2 EVKMDAEF 9

RESULT 6

A60045

Alzheimer's disease amyloid beta/A4 protein precursor - dog (fragment)

C;Species: Canis lupus familiaris (dog)

C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995

C;Accession: A60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: A60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56125

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 2 EVKMDAEF 9

RESULT 7

B60045

Alzheimer's disease amyloid beta/A4 protein precursor - polar bear (fragment)

C;Species: Ursus maritimus (polar bear)

C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999

C;Accession: B60045

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: B60045

A;Molecule type: mRNA

A;Residues: 1-57 <JOH>

A;Cross-references: EMBL:X56128; NID:g2165; PIDN:CAA39593.1; PID:g2166

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 8

PQ0438

Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)

C;Species: *Oryctolagus cuniculus* (domestic rabbit)

C;Date: 30-Sep-1993 #sequence_revision 19-Oct-1995 #text_change 19-Oct-1995

C;Accession: PQ0438; C60045

R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.

Biochem. Biophys. Res. Commun. 188, 905-911, 1992

A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.

A;Reference number: PQ0438; MUID:93075180; PMID:1445331

A;Accession: PQ0438

A;Molecule type: DNA

A;Residues: 1-82 <DAV>

A;Cross-references: GB:M83558; GB:M83657

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: C60045

A;Molecule type: mRNA

A;Residues: 12-68 <JOH>

A;Cross-references: EMBL:X56129

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

Query Match 100.0%; Score 40; DB 2; Length 82;
Best Local Similarity 100.0%; Pred. No. 0.066;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 13 EVKMDAEF 20

RESULT 9

A49795

Alzheimer's disease amyloid beta protein precursor - crab-eating macaque

C;Species: *Macaca fascicularis* (crab-eating macaque)

C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999

C;Accession: A49795

R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.

Am. J. Pathol. 138, 1423-1435, 1991

A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.

A;Reference number: A49795; MUID:91273117; PMID:1905108
A;Accession: A49795
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-695 <POD>
A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing

Query Match 100.0%; Score 40; DB 1; Length 695;
Best Local Similarity 100.0%; Pred. No. 0.69;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 593 EVKMDAEF 600

RESULT 10

A27485

Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse

N;Alternate names: proteinase nexin II

C;Species: Mus musculus (house mouse)

C;Date: 31-Mar-1989 #sequence_revision 31-Mar-1989 #text_change 13-Aug-1999

C;Accession: A27485; S19727; I49485

R;Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.

Biochem. Biophys. Res. Commun. 149, 665-671, 1987

A;Title: Complementary DNA for the mouse homolog of the human amyloid beta
protein precursor.

A;Reference number: A27485; MUID:88106489; PMID:3322280

A;Accession: A27485

A;Molecule type: mRNA

A;Residues: 1-695 <YAM>

A;Cross-references: GB:M18373; NID:g191568; PIDN:AAA37139.1; PID:g309085

A;Experimental source: brain

R;de Strooper, B.; van Leuven, F.; van den Berghe, H.

Biochim. Biophys. Acta 1129, 141-143, 1991

A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is
closer related to its human homolog than previously reported.

A;Reference number: S19727; MUID:92096458; PMID:1756177

A;Accession: S19727

A;Molecule type: mRNA

A;Residues: 1-210,'G',212-220,'S',222-396,'A',398-402,'T',404-448,'A',450-695
<STR>

A;Cross-references: EMBL:X59379

R;Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.

Gene 112, 189-195, 1992

A;Title: Positive and negative regulatory elements for the expression of the
Alzheimer's disease amyloid precursor-encoding gene in mouse.

A;Reference number: I49485; MUID:92209998; PMID:1555768

A;Accession: I49485

A;Status: translated from GB/EMBL/DDBJ

A;Molecule type: DNA

A;Residues: 1-19 <RES>

A;Cross-references: GB:D10603; NID:g220328; PIDN:BAA01456.1; PID:g220329

C;Genetics:

A;Map position: 16C3
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; transmembrane protein

Query Match 100.0%; Score 40; DB 2; Length 695;
Best Local Similarity 100.0%; Pred. No. 0.69;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 593 EVKMDAEF 600

RESULT 11

S00550

Alzheimer's disease amyloid beta protein precursor - rat

N;Alternate names: beta-A4 amyloid protein

C;Species: Rattus norvegicus (Norway rat)

C;Date: 30-Jun-1989 #sequence_revision 30-Jun-1989 #text_change 13-Aug-1999

C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.;
Seeburg, P.H.

EMBO J. 7, 1365-1370, 1988

A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in
rat brain suggests a role in cell contact.

A;Reference number: S00550; MUID:88312583; PMID:2900758

A;Accession: S00550

A;Molecule type: mRNA

A;Residues: 1-695 <SHI>

A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617

R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.
Science 241, 223-226, 1988

A;Title: Amyloid beta protein precursor is possibly a heparan sulfate
proteoglycan core protein.

A;Reference number: A41245; MUID:88264430; PMID:2968652

A;Accession: A41245

A;Molecule type: protein

A;Residues: 18-37, 'X', 39-40, 'X', 42-44 <SCH>

A;Note: evidence for heparan sulfate attachment

R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.
FEBS Lett. 349, 109-116, 1994

A;Title: The beta-A4 amyloid precursor protein binding to copper.

A;Reference number: S46251; MUID:94320627; PMID:7913895

A;Contents: annotation; copper binding sites

A;Note: rat peptides were isolated but not sequenced

R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.
J. Biol. Chem. 266, 8464-8469, 1991

A;Title: Purification and tissue level of the beta-amyloid peptide precursor of
rat brain.

A;Reference number: A39820; MUID:91217087; PMID:1673681

A;Accession: A39820

A;Status: preliminary

A;Molecule type: protein

A;Residues: 18-32 <POT>

A;Experimental source: brain

C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein
F;625-648/Domain: transmembrane #status predicted <TMM>

Query Match 100.0%; Score 40; DB 2; Length 695;
Best Local Similarity 100.0%; Pred. No. 0.69;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 593 EVKMDAEF 600

RESULT 12

QRHUA4

Alzheimer's disease amyloid beta protein precursor [validated] - human
N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)
N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)
C;Species: Homo sapiens (man)
C;Date: 30-Jun-1987 #sequence_revision 28-Jul-1995 #text_change 15-Sep-2000
C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644
R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.
Nucleic Acids Res. 17, 517-522, 1989
A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.
A;Reference number: S02260; MUID:89128427; PMID:2783775
A;Accession: S02260
A;Molecule type: DNA
A;Residues: 1-288,'V',365-770 <LEM1>
A;Cross-references: EMBL:X13466
A;Note: alternative splice form APP(695)
R;Lemaire, H.G.
submitted to the EMBL Data Library, November 1988
A;Reference number: S05194
A;Accession: S05194
A;Molecule type: DNA
A;Residues: 1-14,'VW',17-288,'V',365-770 <LEM2>
A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360
A;Note: alternative splice form APP(695)
R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.
Biochem. Biophys. Res. Commun. 159, 297-304, 1989
A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.
A;Reference number: A32277; MUID:89165870; PMID:2538123
A;Accession: A32277
A;Molecule type: DNA

A;Residues: 1-75 <LAF>
 A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074
 R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.
 Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989
 A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.
 A;Reference number: A33260; MUID:89392030; PMID:2675837
 A;Accession: A33260
 A;Molecule type: DNA
 A;Residues: 656-737 <JOH>
 A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865
 R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.
 Biochem. Biophys. Res. Commun. 170, 301-307, 1990
 A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.
 A;Reference number: A35486; MUID:90321244; PMID:2196878
 A;Accession: A35486
 A;Molecule type: DNA
 A;Residues: 672-710 <PRE1>
 A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
 Gene 87, 257-263, 1990
 A;Title: Genomic organization of the human amyloid beta-protein precursor gene.
 A;Reference number: I39451; MUID:90236318; PMID:2110105
 A;Accession: I39452
 A;Status: nucleic acid sequence not shown; translation not shown; translated from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 1-770 <YOS1>
 A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616
 A;Accession: I39451
 A;Status: nucleic acid sequence not shown; translation not shown; translated from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 1-530, 'QWLMPVIPAFWEAKVGR' <YOS2>
 A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
 Gene 102, 291-292, 1991
 A;Reference number: A59020; MUID:91340168; PMID:1908403
 A;Contents: annotation; erratum
 A;Note: revised physical map for reference I39451
 R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.; van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.
 Science 248, 1124-1126, 1990
 A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral hemorrhage, Dutch type.
 A;Reference number: I39453; MUID:90260663; PMID:2111584
 A;Accession: I39453
 A;Status: translated from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 656-737 <LEV>
 A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620
 A;Note: a mutation with 693-Gln is presented

R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.
 Science 254, 97-99, 1991
 A;Title: A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease.
 A;Reference number: I59562; MUID:92022553; PMID:1925564
 A;Accession: I59562
 A;Status: translated from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 689-716,'F',718-737 <MUR>
 A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721
 R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.; Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.; Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma, V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.; Schellenberg, G.D.
 Am. J. Hum. Genet. 51, 998-1014, 1992
 A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds for the APP gene region.
 A;Reference number: A44017; MUID:93035397; PMID:1415269
 A;Accession: A44017
 A;Molecule type: DNA
 A;Residues: 687-692,'G',694-718 <KAM1>
 A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378
 A;Experimental source: familial Alzheimer disease family SB
 A;Note: sequence extracted from NCBI backbone (NCBIP:115374)
 A;Accession: B44017
 A;Molecule type: DNA
 A;Residues: 687-718 <KAM2>
 A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380
 A;Experimental source: familial Alzheimer disease family LIT
 A;Note: sequence extracted from NCBI backbone (NCBIP:115376)
 A;Note: this sequence has a silent mutation
 R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.; Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.
 Nature 325, 733-736, 1987
 A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor.
 A;Reference number: A03134; MUID:87144572; PMID:2881207
 A;Accession: A03134
 A;Molecule type: mRNA
 A;Residues: 1-288,'V',365-770 <KAN>
 A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526
 A;Note: alternative splice form APP(695)
 R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.
 Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987
 A;Title: Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides.
 A;Reference number: A29030; MUID:87231971; PMID:3035574
 A;Accession: A29030
 A;Molecule type: mRNA
 A;Residues: 284-288,'V',365-646,'E',648-770 <ROB>
 A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540
 A;Note: the authors translated the codon GAG for residue 647 as Asp
 R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.
 Science 235, 877-880, 1987
 A;Title: Characterization and chromosomal localization of a cDNA encoding brain amyloid of Alzheimer's disease.

A;Reference number: A47584; MUID:87120328; PMID:3810169
 A;Accession: A47584
 A;Molecule type: mRNA
 A;Residues: 674-756,'S',758-770 <GOL>
 A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707
 A;Experimental source: brain
 R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop, P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.
 Science 235, 880-884, 1987
 A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage near the Alzheimer locus.
 A;Reference number: A47585; MUID:87120329; PMID:2949367
 A;Accession: A47585
 A;Molecule type: mRNA
 A;Residues: 674-703 <TAN1>
 A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958
 R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang, J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.
 EMBO J. 7, 949-957, 1988
 A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.
 A;Reference number: S02638; MUID:88296437; PMID:2900137
 A;Accession: S02638
 A;Molecule type: mRNA
 A;Residues: 672-678 <DYR>
 R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.
 Nature 331, 528-530, 1988
 A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.
 A;Reference number: S00707; MUID:88122640; PMID:2893290
 A;Accession: S00707
 A;Molecule type: mRNA
 A;Residues: 286-344,'I',365-366 <TAN2>
 A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612
 A;Experimental source: promyelocytic leukemia cell line HL60
 A;Note: alternative splice form APP(751)
 R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.
 Nature 331, 525-527, 1988
 A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.
 A;Reference number: S00925; MUID:88122639; PMID:2893289
 A;Accession: S00925
 A;Molecule type: mRNA
 A;Residues: 1-344,'I',365-770 <PO2>
 A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721
 A;Note: alternative splice form APP(751)
 R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.
 Nature 331, 530-532, 1988
 A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.
 A;Reference number: A38949; MUID:88122641; PMID:2893291
 A;Accession: A38949
 A;Molecule type: mRNA
 A;Residues: 287-367 <KIT>

A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611
A;Experimental source: glioblastoma cell line
A;Note: alternative splice form APP(770)
R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.
Brain Res. Mol. Brain Res. 4, 121-131, 1988
A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.
A;Reference number: A30320
A;Accession: A30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-770 <VIT1>
A;Accession: B30320
A;Status: not compared with conceptual translation
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A;Residues: 122-288,'V',365-770 <VIT2>
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A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 606-770 <VIT3>
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.
A;Reference number: A31087; MUID:88124954; PMID:2893379
A;Accession: A31087
A;Molecule type: mRNA
A;Residues: 507-770 <ZAI>
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser
A;Note: the cited Genbank accession number, J03594, is not in release 101.0
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

Query Match 100.0%; Score 40; DB 1; Length 770;
Best Local Similarity 100.0%; Pred. No. 0.77;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db 668 EVKMDAEF 675

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protein F13A2.1 [imported] - Caenorhabditis elegans
C;Species: Caenorhabditis elegans
C;Date: 10-May-2001 #sequence_revision 10-May-2001 #text_change 10-May-2001
C;Accession: E89026
R;anonymous, The C. elegans Sequencing Consortium.
Science 282, 2012-2018, 1998

A;Title: Genome sequence of the nematode *C. elegans*: a platform for investigating biology.
 A;Reference number: A75000; MUID:99069613; PMID:9851916
 A;Note: see websites genome.wustl.edu/gsc/C_elegans/ and www_sanger.ac.uk/Projects/C_elegans/ for a list of authors
 A;Note: published errata appeared in Science 283, 35, 1999; Science 283, 2103, 1999; and Science 285, 1493, 1999
 A;Accession: E89026
 A;Status: preliminary
 A;Molecule type: DNA
 A;Residues: 1-142 <STO>
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 A;Gene: F13A2.1
 A;Map position: 5

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RESULT 14

JH0773

Alzheimer's disease amyloid beta protein precursor - African clawed frog
 C;Species: *Xenopus laevis* (African clawed frog)
 C;Date: 10-Jun-1993 #sequence_revision 10-Jun-1993 #text_change 13-Aug-1999
 C;Accession: JH0773
 R;Okado, H.; Okamoto, H.
 Biochem. Biophys. Res. Commun. 189, 1561-1568, 1992
 A;Title: A *Xenopus* homologue of the human beta-amyloid precursor protein: developmental regulation of its gene expression.
 A;Reference number: JH0773; MUID:93129227; PMID:1282805
 A;Accession: JH0773
 A;Molecule type: mRNA
 A;Residues: 1-747 <OKA>
 A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151
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 C;Keywords: alternative splicing; amyloid
 F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

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RESULT 15

AF0358

conserved hypothetical protein YPO2947 [imported] - *Yersinia pestis* (strain C092)

C;Species: *Yersinia pestis*

C;Date: 02-Nov-2001 #sequence_revision 02-Nov-2001 #text_change 23-Dec-2002

C;Accession: AF0358

R;Parkhill, J.; Wren, B.W.; Thomson, N.R.; Titball, R.W.; Holden, M.T.G.; Prentice, M.B.; Sebaihia, M.; James, K.D.; Churcher, C.; Mungall, K.L.; Baker, S.; Basham, D.; Bentley, S.D.; Brooks, K.; Cerdeno-Tarraga, A.M.; Chillingworth, T.; Cronin, A.; Davies, R.M.; Davis, P.; Dougan, G.; Feltwell, T.; Hamlin, N.; Holroyd, S.; Jagels, K.; Leather, S.; Karlyshev, A.V.; Moule, S.; Oyston, P.C.F.; Quail, M.; Rutherford, K.; Simmonds, M.; Skelton, J.; Stevens, K.; Whitehead, S.; Barrell, B.G.

Nature 413, 523-527, 2001

A;Title: Genome sequence of *Yersinia pestis*, the causative agent of plague.

A;Reference number: AB0001; MUID:21470413; PMID:11586360

A;Accession: AF0358

A;Status: preliminary

A;Molecule type: DNA

A;Residues: 1-626 <KUR>

A;Cross-references: GB:AL590842; PIDN:CAC92193.1; PID:g15980905; GSPDB:GN00175

C;Genetics:

A;Gene: YPO2947

C;Superfamily: uncharacterized conserved protein

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| | | :: : | |
| Db | 61 | QIKLDAEF | 68 |

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Job time : 2.73423 secs

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: January 21, 2004, 09:25:15 ; Search time 1.60612 Seconds
(without alignments)
1018.511 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 762491 seqs, 204481190 residues

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Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : Published_Applications_AA:*
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Pred. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,
and is derived by analysis of the total score distribution.

SUMMARIES

| Result | | % | Query | | | | | |
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| No. | Score | Match | Length | DB | ID | | | Description |

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| 2 | 40 | 100.0 | 8 | 9 | US-09-795-847-67 | Sequence 67, Appl |
| 3 | 40 | 100.0 | 8 | 9 | US-09-794-743-67 | Sequence 67, Appl |
| 4 | 40 | 100.0 | 8 | 9 | US-09-794-748-67 | Sequence 67, Appl |
| 5 | 40 | 100.0 | 8 | 9 | US-09-794-925-67 | Sequence 67, Appl |
| 6 | 40 | 100.0 | 8 | 9 | US-09-681-442-67 | Sequence 67, Appl |
| 7 | 40 | 100.0 | 8 | 11 | US-09-869-414-67 | Sequence 67, Appl |
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| 23 | 40 | 100.0 | 10 | 15 | US-10-032-818-7 | Sequence 7, Appli |
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| 32 | 40 | 100.0 | 13 | 12 | US-10-337-075-2 | Sequence 2, Appli |
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| 37 | 40 | 100.0 | 13 | 15 | US-10-171-343-2 | Sequence 2, Appli |
| 38 | 40 | 100.0 | 13 | 15 | US-10-264-707-2 | Sequence 2, Appli |
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ALIGNMENTS

RESULT 1

US-09-794-927-67

; Sequence 67, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

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; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/794,927
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-794-927-67

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Best Local Similarity 100.0%; Pred. No. 6.7e+05;
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Db      1 EVKMDAEF 8

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; Patent No. US20010018208A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280DE
; CURRENT APPLICATION NUMBER: US/09/795,847
; CURRENT FILING DATE: 2001-02-28

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; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
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; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-795-847-67

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Best Local Similarity 100.0%; Pred. No. 6.7e+05;
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; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280BC
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; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73

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US-09-794-743-67

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Best Local Similarity 100.0%; Pred. No. 6.7e+05;
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US-09-794-748-67

; Sequence 67, Application US/09794748
; Patent No. US20020037315A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND

; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280JL
; CURRENT APPLICATION NUMBER: US/09/794,748
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
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; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-794-748-67

Query Match 100.0%; Score 40; DB 9; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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; Sequence 67, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

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; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 67

; LENGTH: 8

; TYPE: PRT

; ORGANISM: Artificial Sequence

; FEATURE:

; OTHER INFORMATION: Description of Artificial Sequence: Peptide

US-09-794-925-67

Query Match 100.0%; Score 40; DB 9; Length 8;

Best Local Similarity 100.0%; Pred. No. 6.7e+05;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||

Db 1 EVKMDAEF 8

RESULT 6

US-09-681-442-67

; Sequence 67, Application US/09681442

; Patent No. US20020081634A1

; GENERAL INFORMATION:

```

; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/681,442
; CURRENT FILING DATE: 2001-04-05
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-681-442-67

```

```

Query Match          100.0%; Score 40; DB 9; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches      8; Conservative    0; Mismatches    0; Indels      0; Gaps      0;

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```

Qy      1 EVKMDAEF 8
        |||||
Db      1 EVKMDAEF 8

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RESULT 7
US-09-869-414-67
; Sequence 67, Application US/09869414
; Publication No. US20030077226A1
; GENERAL INFORMATION:
; APPLICANT: Beinkowski et al.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280M
; CURRENT APPLICATION NUMBER: US/09/869,414
; CURRENT FILING DATE: 2001-06-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133

```



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; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-869-414-67
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```
Query Match          100.0%; Score 40; DB 11; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches      8; Conservative    0; Mismatches    0; Indels      0; Gaps      0;
```

```
Qy      1 EVKMDAEF 8
        |||||
Db      1 EVKMDAEF 8
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RESULT 8

US-10-427-208-52

; Sequence 52, Application US/10427208

; Publication No. US2003020055A1

; GENERAL INFORMATION:

; APPLICANT: Merck & Co., Inc.

; APPLICANT: Hazuda, Daria J

; APPLICANT: Chen Dodson, Elizabeth

; APPLICANT: Lai, Ming-Tain

; APPLICANT: Xu, Min

; APPLICANT: Shi, Xiao-Ping

; APPLICANT: Simon, Adam J.

; APPLICANT: Wu, Guoxin

; APPLICANT: Li, Yueming

; APPLICANT: Register, Robert B.

; TITLE OF INVENTION: ASSAYS USING AMYLOID PRECURSOR PROTEINS WITH MODIFIED

; TITLE OF INVENTION: BETA-SECRETASE CLEAVAGE SITES TO MONITOR BETA-SECRETASE

ACTIVITY

; FILE REFERENCE: 21052

; CURRENT APPLICATION NUMBER: US/10/427,208

; CURRENT FILING DATE: 2003-04-30

; NUMBER OF SEQ ID NOS: 75

; SOFTWARE: PatentIn version 3.2

; SEQ ID NO 52

; LENGTH: 8

; TYPE: PRT

; ORGANISM: Homo sapiens

US-10-427-208-52

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Query Match          100.0%; Score 40; DB 12; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches      8; Conservative    0; Mismatches    0; Indels      0; Gaps      0;
```

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 1 EVKMDAEF 8

RESULT 9

US-10-066-319-3

; Sequence 3, Application US/10066319
; Publication No. US20030147810A1
; GENERAL INFORMATION:
; APPLICANT: Ross, Brian D.
; APPLICANT: Rehemtulla, Alnawaz
; TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR REPORTING
; TITLE OF INVENTION: OF PROTEASE ACTIVITY WITHIN THE SECRETORY PATHWAY
; FILE REFERENCE: 11203-007001
; CURRENT APPLICATION NUMBER: US/10/066,319
; CURRENT FILING DATE: 2002-06-17
; NUMBER OF SEQ ID NOS: 18
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 3
; LENGTH: 9
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-066-319-3

Query Match 100.0%; Score 40; DB 12; Length 9;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 10

US-10-016-717-6

; Sequence 6, Application US/10016717
; Publication No. US20020132281A1
; GENERAL INFORMATION:
; APPLICANT: Hook, Vivian Y.H.
; TITLE OF INVENTION: SECRETASES RELATED TO ALZHEIMER'S DEMENTIA
; FILE REFERENCE: P-AS 5031
; CURRENT APPLICATION NUMBER: US/10/016,717
; CURRENT FILING DATE: 2002-03-12
; PRIOR APPLICATION NUMBER: US 09/173,887
; PRIOR FILING DATE: 1998-10-16
; PRIOR APPLICATION NUMBER: US 09/294,987
; PRIOR FILING DATE: 1999-04-20
; NUMBER OF SEQ ID NOS: 6
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 6
; LENGTH: 9
; TYPE: PRT
; ORGANISM: mammalian
US-10-016-717-6

Query Match 100.0%; Score 40; DB 14; Length 9;

Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 2 EVKMDAEF 9

RESULT 11

US-09-794-927-64

; Sequence 64, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/794,927

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 64

; LENGTH: 10

; TYPE: PRT

; ORGANISM: Artificial Sequence

; FEATURE:

; OTHER INFORMATION: Description of Artificial Sequence: synthetic

US-09-794-927-64

Query Match 100.0%; Score 40; DB 9; Length 10;

Best Local Similarity 100.0%; Pred. No. 0.041;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 2 EVKMDAEF 9

RESULT 12

US-09-795-847-64

; Sequence 64, Application US/09795847

```

; Patent No. US20010018208A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280DE
; CURRENT APPLICATION NUMBER: US/09/795,847
; CURRENT FILING DATE: 2001-02-28
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-795-847-64

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```

Query Match          100.0%; Score 40; DB 9; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.041;
Matches      8; Conservative    0; Mismatches    0; Indels      0; Gaps      0;

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```

Qy      1 EVKMDAEF 8
        |||||
Db      2 EVKMDAEF 9

```

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RESULT 13
US-09-794-743-64
; Sequence 64, Application US/09794743
; Patent No. US20010021391A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR

```

```
; FILE REFERENCE: 28341/6280BC
; CURRENT APPLICATION NUMBER: US/09/794,743
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-743-64
```

```
Query Match          100.0%; Score 40; DB 9; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.041;
Matches      8; Conservative    0; Mismatches    0; Indels    0; Gaps    0;
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```
Qy      1 EVKMDAEF 8
        |||||
Db      2 EVKMDAEF 9
```

RESULT 14

US-09-794-748-64

```
; Sequence 64, Application US/09794748
; Patent No. US20020037315A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280JL
; CURRENT APPLICATION NUMBER: US/09/794,748
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
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; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-748-64

Query Match 100.0%; Score 40; DB 9; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.041;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 2 EVKMDAEF 9

RESULT 15
US-09-796-264-4
; Sequence 4, Application US/09796264
; Patent No. US20020049303A1
; GENERAL INFORMATION:
; APPLICANT: Tang, Jordan J.N.
; APPLICANT: Lin, Xinli
; APPLICANT: Koelsch, Gerald
; TITLE OF INVENTION: Catalytically Active Recombinant Memapsin and Methods
; TITLE OF INVENTION: of Use Thereof
; FILE REFERENCE: OMRF 179
; CURRENT APPLICATION NUMBER: US/09/796,264
; CURRENT FILING DATE: 2001-02-28
; PRIOR APPLICATION NUMBER: 09/604,608
; PRIOR FILING DATE: 2000-06-27
; PRIOR APPLICATION NUMBER: 60/168,060
; PRIOR FILING DATE: 1999-11-30
; PRIOR APPLICATION NUMBER: 60/177,836
; PRIOR FILING DATE: 2000-01-25
; PRIOR APPLICATION NUMBER: 60/178,368
; PRIOR FILING DATE: 2000-01-27
; PRIOR APPLICATION NUMBER: 60/210,292
; PRIOR FILING DATE: 2000-06-08
; NUMBER OF SEQ ID NOS: 31
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-796-264-4

Query Match 100.0%; Score 40; DB 9; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.041;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 | | | | | | | |
Db 2 EVKMDAEF 9

Search completed: January 21, 2004, 09:41:42
Job time : 1.60612 secs

| | | $\frac{9}{8}$ | | | | | |
|--------|-------|---------------|----|----|--|-------------|--|
| Result | | Query | | | | | |
| No. | Score | Match Length | DB | ID | | Description | |

| | | | | | | |
|----|----|-------|------|----|--------|--------------------|
| 1 | 40 | 100.0 | 35 | 4 | Q8WZ99 | Q8wz99 homo sapien |
| 2 | 40 | 100.0 | 79 | 11 | O35463 | O35463 cricetus |
| 3 | 40 | 100.0 | 82 | 4 | Q16020 | Q16020 homo sapien |
| 4 | 40 | 100.0 | 82 | 4 | Q16014 | Q16014 homo sapien |
| 5 | 40 | 100.0 | 82 | 4 | Q16019 | Q16019 homo sapien |
| 6 | 40 | 100.0 | 113 | 13 | Q8JH58 | Q8jh58 chelydra se |
| 7 | 40 | 100.0 | 218 | 11 | Q8BPV5 | Q8bpv5 mus musculu |
| 8 | 40 | 100.0 | 384 | 11 | Q8BPC7 | Q8bpc7 mus musculu |
| 9 | 40 | 100.0 | 534 | 13 | O93296 | O93296 gallus gall |
| 10 | 40 | 100.0 | 569 | 13 | Q9PVL1 | Q9pvl1 gallus gall |
| 11 | 40 | 100.0 | 607 | 11 | Q99K32 | Q99k32 mus musculu |
| 12 | 40 | 100.0 | 695 | 11 | Q60496 | Q60496 cavia sp. p |
| 13 | 40 | 100.0 | 695 | 11 | P97487 | P97487 mus musculu |
| 14 | 40 | 100.0 | 695 | 13 | Q9DGJ8 | Q9dgj8 gallus gall |
| 15 | 40 | 100.0 | 751 | 13 | Q9DGJ7 | Q9dgj7 gallus gall |
| 16 | 40 | 100.0 | 770 | 6 | Q9TUI0 | Q9tui0 sus scrofa |
| 17 | 35 | 87.5 | 2148 | 5 | Q8IPL5 | Q8ipl5 drosophila |
| 18 | 34 | 85.0 | 142 | 5 | O16896 | O16896 caenorhabdi |
| 19 | 34 | 85.0 | 693 | 13 | Q98SG0 | Q98sg0 xenopus lae |
| 20 | 34 | 85.0 | 695 | 13 | Q98SF9 | Q98sf9 xenopus lae |
| 21 | 34 | 85.0 | 747 | 13 | Q91963 | Q91963 xenopus. ap |
| 22 | 33 | 82.5 | 317 | 17 | Q96ZT2 | Q96zt2 sulfolobus |
| 23 | 33 | 82.5 | 423 | 2 | O52379 | O52379 ralstonia s |
| 24 | 33 | 82.5 | 423 | 2 | Q45693 | Q45693 burkholderi |
| 25 | 33 | 82.5 | 626 | 16 | Q8ZCN4 | Q8zcn4 yersinia pe |
| 26 | 32 | 80.0 | 286 | 2 | Q8VNV1 | Q8vnv1 chlorobium |
| 27 | 32 | 80.0 | 289 | 2 | Q8VNV3 | Q8vnv3 chlorobium |
| 28 | 32 | 80.0 | 289 | 2 | Q8VNW1 | Q8vnw1 chlorobium |
| 29 | 32 | 80.0 | 289 | 2 | Q8VNV2 | Q8vnv2 chlorobium |
| 30 | 32 | 80.0 | 289 | 2 | Q8VL89 | Q8vl89 chlorobium |
| 31 | 32 | 80.0 | 289 | 2 | Q8VLL7 | Q8vll7 chlorobium |
| 32 | 32 | 80.0 | 338 | 2 | Q9AL67 | Q9al67 chlorobium |
| 33 | 32 | 80.0 | 350 | 2 | Q9AL73 | Q9al73 chlorobium |
| 34 | 32 | 80.0 | 350 | 2 | Q9AL69 | Q9al69 chlorobium |
| 35 | 32 | 80.0 | 350 | 2 | Q9AL72 | Q9al72 chlorobium |
| 36 | 32 | 80.0 | 426 | 17 | Q9V2P8 | Q9v2p8 pyrococcus |
| 37 | 32 | 80.0 | 630 | 2 | Q93IK4 | Q93ik4 vibrio sp. |
| 38 | 32 | 80.0 | 859 | 3 | Q9HFI9 | Q9hfi9 neurospora |
| 39 | 31 | 77.5 | 119 | 17 | Q8ZZP0 | Q8zzp0 pyrobaculum |
| 40 | 31 | 77.5 | 161 | 16 | Q98FZ2 | Q98fz2 rhizobium l |
| 41 | 31 | 77.5 | 282 | 5 | O02335 | O02335 caenorhabdi |
| 42 | 31 | 77.5 | 328 | 11 | Q9CZC7 | Q9czc7 mus musculu |
| 43 | 31 | 77.5 | 328 | 11 | Q8BPI1 | Q8bpil mus musculu |
| 44 | 31 | 77.5 | 705 | 16 | Q8E8V4 | Q8e8v4 shewanella |
| 45 | 31 | 77.5 | 1209 | 10 | Q94FG7 | Q94fg7 chlamydomon |

ALIGNMENTS

RESULT 1

Q8WZ99

ID Q8WZ99 PRELIMINARY; PRT; 35 AA.

AC Q8WZ99;

DT 01-MAR-2002 (TrEMBLrel. 20, Created)

DT 01-MAR-2002 (TrEMBLrel. 20, Last sequence update)

DT 01-MAR-2002 (TrEMBLrel. 20, Last annotation update)

DE Amyloid protein (Fragment).
 GN APP.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Wakutani Y., Ninomiya H., Iwata H., Tanaka S., Urakami K., Adachi Y.,
 RA Wada-Isoe K., Yamagata K., Ohono K., Tsubuki S., Saido T.,
 RA Hashimoto T., Iwatsubo T., Nakashima K.;
 RT "Novel missense mutation (D678N) of amyloid precursor protein gene in
 RT a Japanese pedigree of familial Alzheimer's disease."
 RL Submitted (JUL-2001) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; AB066441; BAB71958.1; -.
 FT NON_TER 1 1
 FT NON_TER 35 35
 SQ SEQUENCE 35 AA; 4084 MW; 49D7D17289743B71 CRC64;

Query Match 100.0%; Score 40; DB 4; Length 35;
 Best Local Similarity 100.0%; Pred. No. 0.14;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 13 EVKMDAEF 20

RESULT 2

O35463

ID O35463 PRELIMINARY; PRT; 79 AA.
 AC O35463;
 DT 01-JAN-1998 (TrEMBLrel. 05, Created)
 DT 01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
 DT 01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
 DE Alzheimer's amyloid beta protein (Fragment).
 GN BETA APP.
 OS Cricetulus griseus (Chinese hamster).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
 OC Cricetulus.
 OX NCBI_TaxID=10029;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Sambamurti K., Pinnix I., Gandhi S.;
 RL Submitted (OCT-1997) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; AF030413; AAB86608.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 FT NON_TER 1 1
 FT NON_TER 79 79
 SQ SEQUENCE 79 AA; 8538 MW; 37F2C6C3BFF3F597 CRC64;

Query Match 100.0%; Score 40; DB 11; Length 79;
 Best Local Similarity 100.0%; Pred. No. 0.31;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 17 EVKMDAEF 24

RESULT 3

Q16020

ID Q16020 PRELIMINARY; PRT; 82 AA.
AC Q16020;
DT 01-NOV-1996 (TrEMBLrel. 01, Created)
DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT 01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE Beta-amyloid peptide (Fragment).
GN BETA APP.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=93236601; PubMed=8476439;
RA Denman R.B., Rosenzwaig R., Miller D.L.;
RT "A system for studying the effect(s) of familial Alzheimer disease
RT mutations on the processing of the beta-amyloid peptide precursor.";
RL Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR EMBL; S61383; AAB26265.2; -.
DR HSSP; P05067; 1BA4.
DR InterPro; IPR001255; Beta-APP.
DR Pfam; PF03494; Beta-APP; 1.
FT NON_TER 1 1
FT NON_TER 82 82
SQ SEQUENCE 82 AA; 8882 MW; F534AA5AE5D9230A CRC64;

Query Match 100.0%; Score 40; DB 4; Length 82;
Best Local Similarity 100.0%; Pred. No. 0.32;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 14 EVKMDAEF 21

RESULT 4

Q16014

ID Q16014 PRELIMINARY; PRT; 82 AA.
AC Q16014;
DT 01-NOV-1996 (TrEMBLrel. 01, Created)
DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT 01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE Beta-amyloid peptide (Fragment).
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.

RX MEDLINE=93236601; PubMed=8476439;
 RA Denman R.B., Rosenzwaig R., Miller D.L.;
 RT "A system for studying the effect(s) of familial Alzheimer disease
 mutations on the processing of the beta-amyloid peptide precursor.";
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).
 DR EMBL; S60721; AAB26263.2; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 FT NON_TER 1 1
 FT NON_TER 82 82
 SQ SEQUENCE 82 AA; 8972 MW; F534AA5B3EA9230A CRC64;

Query Match 100.0%; Score 40; DB 4; Length 82;
 Best Local Similarity 100.0%; Pred. No. 0.32;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |
 Db 14 EVKMDAEF 21

RESULT 5

Q16019

ID Q16019 PRELIMINARY; PRT; 82 AA.
 AC Q16019;
 DT 01-NOV-1996 (TrEMBLrel. 01, Created)
 DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
 DT 01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
 DE Beta-amyloid peptide (Fragment).
 GN BETA APP.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=93236601; PubMed=8476439;
 RA Denman R.B., Rosenzwaig R., Miller D.L.;
 RT "A system for studying the effect(s) of familial Alzheimer disease
 mutations on the processing of the beta-amyloid peptide precursor.";
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).
 DR EMBL; S61380; AAB26264.2; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 FT NON_TER 1 1
 FT NON_TER 82 82
 SQ SEQUENCE 82 AA; 8938 MW; F534AA50E579230A CRC64;

Query Match 100.0%; Score 40; DB 4; Length 82;
 Best Local Similarity 100.0%; Pred. No. 0.32;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |
 Db 14 EVKMDAEF 21

RESULT 6

Q8JH58

ID Q8JH58 PRELIMINARY; PRT; 113 AA.
AC Q8JH58;
DT 01-OCT-2002 (TrEMBLrel. 22, Created)
DT 01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DT 01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE Amyloid beta protein (Fragment).
OS Chelydra serpentina serpentina (common snapping turtle).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Testudines; Cryptodira; Testudinoidea; Chelydridae; Chelydra.
OX NCBI_TaxID=134619;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=21876906; PubMed=11882478;
RA Trudeau V.L., Chiu S., Kennedy S.W., Brooks R.J.;
RT "Octylphenol (OP) alters the expression of members of the amyloid
RT protein family in the hypothalamus of the snapping turtle, Chelydra
RT serpentina serpentina.";
RL Environ. Health Perspect. 110:269-275(2002).
DR EMBL; AF541917; AAN04908.1; -.
DR InterPro; IPR001868; A4_APP.
DR InterPro; IPR001255; Beta-APP.
DR Pfam; PF03494; Beta-APP; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR PROSITE; PS00320; A4_INTRA; 1.
FT NON_TER 1 1
SQ SEQUENCE 113 AA; 12750 MW; 72515C930496E053 CRC64;

Query Match 100.0%; Score 40; DB 13; Length 113;
Best Local Similarity 100.0%; Pred. No. 0.44;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 11 EVKMDAEF 18

RESULT 7

Q8BPV5

ID Q8BPV5 PRELIMINARY; PRT; 218 AA.
AC Q8BPV5;
DT 01-MAR-2003 (TrEMBLrel. 23, Created)
DT 01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT 01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE Amyloid beta (Fragment).
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=C57BL/6J; TISSUE=Lung;
RX MEDLINE=22354683; PubMed=12466851;
RA The FANTOM Consortium,

RA the RIKEN Genome Exploration Research Group Phase I & II Team;
RT "Analysis of the mouse transcriptome based on functional annotation of
RT 60,770 full-length cDNAs.";
RL Nature 420:563-573(2002).
DR EMBL; AK052448; BAC34997.1; -.
FT NON_TER 1 1
SQ SEQUENCE 218 AA; 24118 MW; 95B55AFDAE1D0EF5 CRC64;

Query Match 100.0%; Score 40; DB 11; Length 218;
Best Local Similarity 100.0%; Pred. No. 0.86;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 116 EVKMDAEF 123

RESULT 8

Q8BPC7

ID Q8BPC7 PRELIMINARY; PRT; 384 AA.
AC Q8BPC7;
DT 01-MAR-2003 (TrEMBLrel. 23, Created)
DT 01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT 01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE Amyloid beta (Fragment).
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=C57BL/6J; TISSUE=Head;
RX MEDLINE=22354683; PubMed=12466851;
RA The FANTOM Consortium,
RA the RIKEN Genome Exploration Research Group Phase I & II Team;
RT "Analysis of the mouse transcriptome based on functional annotation of
RT 60,770 full-length cDNAs.";
RL Nature 420:563-573(2002).
DR EMBL; AK076506; BAC36369.1; -.
FT NON_TER 1 1
SQ SEQUENCE 384 AA; 43990 MW; A81B1AD8AE683173 CRC64;

Query Match 100.0%; Score 40; DB 11; Length 384;
Best Local Similarity 100.0%; Pred. No. 1.5;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 282 EVKMDAEF 289

RESULT 9

O93296

ID O93296 PRELIMINARY; PRT; 534 AA.
AC O93296;
DT 01-NOV-1998 (TrEMBLrel. 08, Created)
DT 01-NOV-1998 (TrEMBLrel. 08, Last sequence update)

DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
 DE Amyloid protein (Fragment).
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=98337885; PubMed=9671674;
 RA Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,
 RA Milligan C.E.;
 RT "Increased production of amyloid precursor protein provides a
 RT substrate for caspase-3 in dying motoneurons."
 RL J. Neurosci. 18:5869-5880(1998).
 DR EMBL; AF042098; AAC25052.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 FT NON_TER 1 1
 SQ SEQUENCE 534 AA; 60597 MW; FB53ECC2E66D4C92 CRC64;

Query Match 100.0%; Score 40; DB 13; Length 534;
 Best Local Similarity 100.0%; Pred. No. 2.1;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 432 EVKMDAEF 439

RESULT 10

Q9PVL1

ID Q9PVL1 PRELIMINARY; PRT; 569 AA.
 AC Q9PVL1;
 DT 01-MAY-2000 (TrEMBLrel. 13, Created)
 DT 01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
 DT 01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
 DE Amyloid protein (Fragment).
 GN APP.
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Brain;
 RA Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
 RT "What the evolution of the amyloid protein precursor supergene family
 RT tells us about its function."
 RL Neurochem. Int. 0:0-0(2000).

DR EMBL; AF030341; AAF12698.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 FT NON_TER 1 1
 SQ SEQUENCE 569 AA; 64753 MW; 0AB8BB851863A19D CRC64;

Query Match 100.0%; Score 40; DB 13; Length 569;
 Best Local Similarity 100.0%; Pred. No. 2.3;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 468 EVKMDAEF 475

RESULT 11

Q99K32

ID Q99K32 PRELIMINARY; PRT; 607 AA.
 AC Q99K32;
 DT 01-JUN-2001 (TrEMBLrel. 17, Created)
 DT 01-JUN-2001 (TrEMBLrel. 17, Last sequence update)
 DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
 DE Hypothetical 68.4 kDa protein (Fragment).
 GN APP.
 OS Mus musculus (Mouse).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 OX NCBI_TaxID=10090;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Strausberg R.;
 RL Submitted (MAR-2001) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; BC005490; AAH05490.1; -.
 DR HSSP; P05067; 1AAP.
 DR MGD; MGI:88059; App.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS00279; BPTI_KUNITZ_2; 1.
 KW Hypothetical protein; Protease inhibitor; Serine protease inhibitor.
 FT NON_TER 1 1

SQ SEQUENCE 607 AA; 68391 MW; BF802214CBA7D172 CRC64;

Query Match 100.0%; Score 40; DB 11; Length 607;
Best Local Similarity 100.0%; Pred. No. 2.4;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 505 EVKMDAEF 512

RESULT 12

Q60496

ID Q60496 PRELIMINARY; PRT; 695 AA.
AC Q60496;
DT 01-NOV-1996 (TrEMBLrel. 01, Created)
DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE Putative amyloid precursor protein.
OS Cavia sp.
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX NCBI_TaxID=10143;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=97236426; PubMed=9116031;
RA Beck M., Mueller D., Bigl V.;
RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT alternative splicing."
RL Biochim. Biophys. Acta 1351:17-21(1997).
DR EMBL; X97631; CAA66230.1; -.
DR HSSP; P05067; 1BA4.
DR InterPro; IPR001868; A4_APP.
DR InterPro; IPR001255; Beta-APP.
DR Pfam; PF02177; A4_EXTRA; 1.
DR Pfam; PF03494; Beta-APP; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR SMART; SM00006; A4_EXTRA; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
SQ SEQUENCE 695 AA; 78701 MW; 5196A0C4017F16AB CRC64;

Query Match 100.0%; Score 40; DB 11; Length 695;
Best Local Similarity 100.0%; Pred. No. 2.8;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 593 EVKMDAEF 600

RESULT 13

P97487

ID P97487 PRELIMINARY; PRT; 695 AA.
AC P97487; P97942;
DT 01-MAY-1997 (TrEMBLrel. 03, Created)

DT 01-MAY-1997 (TrEMBLrel. 03, Last sequence update)
 DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
 DE Hippocampal amyloid protein.
 GN APP.
 OS Mus musculus (Mouse).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 OX NCBI_TaxID=10090;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN=SAMP8; TISSUE=Hippocampus;
 RA Flood J.F., Kumar V.B., Sasser T., Word I., Morley J.E.;
 RL Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
 RN [2]
 RP SEQUENCE OF 581-662 FROM N.A.
 RC STRAIN=129SV;
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
 RA Loring J.F., Goate A.M.;
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; U84012; AAB41502.1; -.
 DR EMBL; U82624; AAB40919.1; -.
 DR HSSP; P05067; 1MWP.
 DR MGD; MGI:88059; App.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 SQ SEQUENCE 695 AA; 78414 MW; 9A5FBE2ED261236E CRC64;

Query Match 100.0%; Score 40; DB 11; Length 695;
 Best Local Similarity 100.0%; Pred. No. 2.8;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 593 EVKMDAEF 600

RESULT 14

Q9DGJ8

ID Q9DGJ8 PRELIMINARY; PRT; 695 AA.
 AC Q9DGJ8;
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
 DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
 DE Beta-amyloid precursor protein 695 isoform.
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN [1]
 RP SEQUENCE FROM N.A.

RA Sarasa M., Rodolosse A., Sorribas V.;
 RT "Cloning of full-length chicken beta-amyloid precursor protein
 RT isoforms.";
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; AF289218; AAG00593.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 SQ SEQUENCE 695 AA; 78565 MW; F201ED02AEC86D95 CRC64;

Query Match 100.0%; Score 40; DB 13; Length 695;
 Best Local Similarity 100.0%; Pred. No. 2.8;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 593 EVKMDAEF 600

RESULT 15

Q9DGJ7

ID Q9DGJ7 PRELIMINARY; PRT; 751 AA.
 AC Q9DGJ7;
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
 DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
 DE Beta-amyloid precursor protein 751 isoform.
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Sarasa M., Rodolosse A., Sorribas V.;
 RT "Cloning of full-length chicken beta-amyloid precursor protein
 RT isoforms.";
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; AF289219; AAG00594.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.

DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW Protease inhibitor; Serine protease inhibitor.
SQ SEQUENCE 751 AA; 84705 MW; E78E9413A8033D84 CRC64;

Query Match 100.0%; Score 40; DB 13; Length 751;
Best Local Similarity 100.0%; Pred. No. 3;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 649 EVKMDAEF 656

Search completed: January 21, 2004, 09:25:11
Job time : 2.65201 secs

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OM protein - protein search, using sw model

Run on: January 21, 2004, 09:15:44 ; Search time 0.397706 Seconds
(without alignments)
945.960 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 127863 seqs, 47026705 residues

Total number of hits satisfying chosen parameters: 127863

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_41:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | % Query | | DB | ID | Description |
|------------|-------|---------|--------|----|------------|--------------------|
| | | Match | Length | | | |
| 1 | 40 | 100.0 | 57 | 1 | A4_URSMA | Q29149 ursus marit |
| 2 | 40 | 100.0 | 58 | 1 | A4_CANFA | Q28280 canis famil |
| 3 | 40 | 100.0 | 58 | 1 | A4_RABIT | Q28748 oryctolagus |
| 4 | 40 | 100.0 | 58 | 1 | A4_SHEEP | Q28757 ovis aries |
| 5 | 40 | 100.0 | 59 | 1 | A4_BOVIN | Q28053 bos taurus |
| 6 | 40 | 100.0 | 751 | 1 | A4_SAISC | Q95241 s amyloid b |
| 7 | 40 | 100.0 | 770 | 1 | A4_CAVPO | Q60495 c amyloid b |
| 8 | 40 | 100.0 | 770 | 1 | A4_HUMAN | P05067 h amyloid b |
| 9 | 40 | 100.0 | 770 | 1 | A4_MACFA | P53601 m amyloid b |
| 10 | 40 | 100.0 | 770 | 1 | A4_MOUSE | P12023 m amyloid b |
| 11 | 40 | 100.0 | 770 | 1 | A4_PIG | P79307 s amyloid b |
| 12 | 40 | 100.0 | 770 | 1 | A4_RAT | P08592 r amyloid b |
| 13 | 32 | 80.0 | 354 | 1 | BCPA_CHLLT | Q46135 chlorobium |
| 14 | 32 | 80.0 | 365 | 1 | BCPA_CHLTE | Q46393 chlorobium |
| 15 | 32 | 80.0 | 1906 | 1 | YFA0_ANASP | Q8ym40 anabaena sp |
| 16 | 31 | 77.5 | 3562 | 1 | PGCV_CHICK | Q90953 gallus gall |
| 17 | 30 | 75.0 | 81 | 1 | RS16_CLOPE | Q8xjp4 clostridium |

| | | | | | | | |
|----|----|------|------|---|------------|--------|-------------|
| 18 | 29 | 72.5 | 84 | 1 | U222_CAEEL | Q9xvz8 | caenorhabdi |
| 19 | 29 | 72.5 | 400 | 1 | YF74_ARCFU | O28698 | archaeoglob |
| 20 | 29 | 72.5 | 452 | 1 | F26_YEAST | P32604 | saccharomyc |
| 21 | 29 | 72.5 | 463 | 1 | YDI4_SCHPO | Q92342 | schizosacch |
| 22 | 29 | 72.5 | 464 | 1 | SPN5_SCHPO | P48010 | schizosacch |
| 23 | 29 | 72.5 | 491 | 1 | RNG_HAEIN | P45175 | haemophilus |
| 24 | 29 | 72.5 | 526 | 1 | SECD_HELPJ | Q9zj66 | helicobacte |
| 25 | 29 | 72.5 | 656 | 1 | V091_FOWPV | O72896 | fowlpox vir |
| 26 | 29 | 72.5 | 871 | 1 | POB1_SCHPO | O74653 | schizosacch |
| 27 | 29 | 72.5 | 949 | 1 | PODK_MESCR | Q42910 | mesembryant |
| 28 | 29 | 72.5 | 4563 | 1 | APB_HUMAN | P04114 | homo sapien |
| 29 | 28 | 70.0 | 197 | 1 | OM26_HAEIN | Q57483 | haemophilus |
| 30 | 28 | 70.0 | 221 | 1 | PBPH_CAEEL | O16264 | caenorhabdi |
| 31 | 28 | 70.0 | 227 | 1 | FA3C_HUMAN | Q92520 | homo sapien |
| 32 | 28 | 70.0 | 227 | 1 | FA3C_MOUSE | Q91vu0 | mus musculu |
| 33 | 28 | 70.0 | 231 | 1 | RNH_STRCO | Q9x7r6 | streptomyce |
| 34 | 28 | 70.0 | 261 | 1 | YN10_ARCFU | O27974 | archaeoglob |
| 35 | 28 | 70.0 | 269 | 1 | T2S1_STRFI | O52512 | streptomyce |
| 36 | 28 | 70.0 | 299 | 1 | YJ52_STRCO | Q9z513 | streptomyce |
| 37 | 28 | 70.0 | 304 | 1 | PH85_KLULA | Q92241 | kluveromyc |
| 38 | 28 | 70.0 | 305 | 1 | PH85_YEAST | P17157 | saccharomyc |
| 39 | 28 | 70.0 | 424 | 1 | EF1A_THEAC | P19486 | thermoplasm |
| 40 | 28 | 70.0 | 424 | 1 | EF1A_THEVO | Q979t1 | thermoplasm |
| 41 | 28 | 70.0 | 673 | 1 | FXO3_HUMAN | O43524 | homo sapien |
| 42 | 28 | 70.0 | 695 | 1 | PARE_CAUCR | O54479 | caulobacter |
| 43 | 28 | 70.0 | 863 | 1 | PHSG_MYCTU | Q10639 | mycobacteri |
| 44 | 28 | 70.0 | 927 | 1 | CC15_SCHPO | Q09822 | schizosacch |
| 45 | 28 | 70.0 | 1017 | 1 | MCM6_YEAST | P53091 | saccharomyc |

ALIGNMENTS

RESULT 1

A4_URSMA

ID A4_URSMA STANDARD; PRT; 57 AA.
AC Q29149;
DT 01-NOV-1997 (Rel. 35, Created)
DT 01-NOV-1997 (Rel. 35, Last sequence update)
DT 30-MAY-2000 (Rel. 39, Last annotation update)
DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE protein (Beta-APP) (A-beta)] (Fragment).
GN APP.
OS Ursus maritimus (Polar bear) (Thalarctos maritimus).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Carnivora; Fissipedia; Ursidae; Ursus.
OX NCBI_TaxID=29073;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=92017079; PubMed=1656157;
RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT "Conservation of the sequence of the Alzheimer's disease amyloid
RT peptide in dog, polar bear and five other mammals by cross-species
RT polymerase chain reaction analysis."
RL Brain Res. Mol. Brain Res. 10:299-305(1991).
CC -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO

CC INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
 CC G(O) (BY SIMILARITY).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -----
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 CC -----
 DR EMBL; X56128; CAA39593.1; -.
 DR PIR; B60045; B60045.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PROSITE; PS00319; A4_EXTRA; PARTIAL.
 DR PROSITE; PS00320; A4_INTRA; PARTIAL.
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.
 FT NON_TER 1 1
 FT CHAIN 6 48 BETA-AMYLOID PROTEIN (POTENTIAL).
 FT DOMAIN <1 33 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 34 57 POTENTIAL.
 FT NON_TER 57 57
 SQ SEQUENCE 57 AA; 6172 MW; 84209D88EBA82DFA CRC64;

Query Match 100.0%; Score 40; DB 1; Length 57;
 Best Local Similarity 100.0%; Pred. No. 0.048;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 2 EVKMDAEF 9

RESULT 2
 A4_CANFA
 ID A4_CANFA STANDARD; PRT; 58 AA.
 AC Q28280;
 DT 01-NOV-1997 (Rel. 35, Created)
 DT 01-NOV-1997 (Rel. 35, Last sequence update)
 DT 30-MAY-2000 (Rel. 39, Last annotation update)
 DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
 DE protein (Beta-APP) (A-beta)] (Fragment).
 GN APP.
 OS Canis familiaris (Dog).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
 OX NCBI_TaxID=9615;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Kidney;
 RX MEDLINE=92017079; PubMed=1656157;
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;

RT "Conservation of the sequence of the Alzheimer's disease amyloid
 RT peptide in dog, polar bear and five other mammals by cross-species
 RT polymerase chain reaction analysis.";
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).
 CC -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
 CC INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
 CC G(O) (BY SIMILARITY).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -----
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 CC -----
 DR EMBL; X56125; CAA39590.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PROSITE; PS00319; A4_EXTRA; PARTIAL.
 DR PROSITE; PS00320; A4_INTRA; PARTIAL.
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.
 FT NON_TER 1 1
 FT CHAIN 7 49 BETA-AMYLOID PROTEIN (POTENTIAL).
 FT DOMAIN <1 34 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 35 58 POTENTIAL.
 FT NON_TER 58 58
 SQ SEQUENCE 58 AA; 6285 MW; 8469D488A2E12DFA CRC64;

Query Match 100.0%; Score 40; DB 1; Length 58;
 Best Local Similarity 100.0%; Pred. No. 0.049;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 3 EVKMDAEF 10

RESULT 3

A4_RABIT

ID A4_RABIT STANDARD; PRT; 58 AA.
 AC Q28748;
 DT 01-NOV-1997 (Rel. 35, Created)
 DT 01-NOV-1997 (Rel. 35, Last sequence update)
 DT 16-OCT-2001 (Rel. 40, Last annotation update)
 DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
 DE protein (Beta-APP) (A-beta)] (Fragment).
 GN APP.
 OS Oryctolagus cuniculus (Rabbit).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Lagomorpha; Leporidae; Oryctolagus.
 OX NCBI_TaxID=9986;
 RN [1]

RP SEQUENCE FROM N.A.
 RC TISSUE=Brain;
 RX MEDLINE=92017079; PubMed=1656157;
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
 RT "Conservation of the sequence of the Alzheimer's disease amyloid
 RT peptide in dog, polar bear and five other mammals by cross-species
 RT polymerase chain reaction analysis."
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).
 CC -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
 CC INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
 CC G(O) (BY SIMILARITY).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -----
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 CC -----
 DR EMBL; X56129; CAA39594.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PROSITE; PS00319; A4_EXTRA; PARTIAL.
 DR PROSITE; PS00320; A4_INTRA; PARTIAL.
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.
 FT NON_TER 1 1
 FT CHAIN 6 48 BETA-AMYLOID PROTEIN (POTENTIAL).
 FT DOMAIN <1 33 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 34 57 POTENTIAL.
 FT DOMAIN 58 >58 CYTOPLASMIC (POTENTIAL).
 FT NON_TER 58 58
 SQ SEQUENCE 58 AA; 6300 MW; F434209D88EBA82D CRC64;

Query Match 100.0%; Score 40; DB 1; Length 58;
 Best Local Similarity 100.0%; Pred. No. 0.049;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 2 EVKMDAEF 9

RESULT 4

A4_SHEEP

ID A4_SHEEP STANDARD; PRT; 58 AA.
 AC Q28757;
 DT 01-NOV-1997 (Rel. 35, Created)
 DT 01-NOV-1997 (Rel. 35, Last sequence update)
 DT 30-MAY-2000 (Rel. 39, Last annotation update)
 DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
 DE protein (Beta-APP) (A-beta)] (Fragment).
 GN APP.

OS Ovis aries (Sheep).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
 OC Bovidae; Caprinae; Ovis.
 OX NCBI_TaxID=9940;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Heart;
 RX MEDLINE=92017079; PubMed=1656157;
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
 RT "Conservation of the sequence of the Alzheimer's disease amyloid
 RT peptide in dog, polar bear and five other mammals by cross-species
 RT polymerase chain reaction analysis.";
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).
 CC -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
 CC INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
 CC G(O) (BY SIMILARITY).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -----
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 CC -----
 DR EMBL; X56130; CAA39595.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PROSITE; PS00319; A4_EXTRA; PARTIAL.
 DR PROSITE; PS00320; A4_INTRA; PARTIAL.
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.
 FT NON_TER 1 1
 FT CHAIN 6 48 BETA-AMYLOID PROTEIN (POTENTIAL).
 FT DOMAIN <1 33 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 34 57 POTENTIAL.
 FT DOMAIN 58 >58 CYTOPLASMIC (POTENTIAL).
 FT NON_TER 58 58
 SQ SEQUENCE 58 AA; 6300 MW; F434209D88EBA82D CRC64;

Query Match 100.0%; Score 40; DB 1; Length 58;
 Best Local Similarity 100.0%; Pred. No. 0.049;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 EVKMDAEF 8
 |||||
 Db 2 EVKMDAEF 9

RESULT 5
 A4_BOVIN
 ID A4_BOVIN STANDARD; PRT; 59 AA.
 AC Q28053;

DT 01-NOV-1997 (Rel. 35, Created)
 DT 01-NOV-1997 (Rel. 35, Last sequence update)
 DT 30-MAY-2000 (Rel. 39, Last annotation update)
 DE Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
 DE protein (Beta-APP) (A-beta)] (Fragment).
 GN APP.
 OS Bos taurus (Bovine).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
 OC Bovidae; Bovinae; Bos.
 OX NCBI_TaxID=9913;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Brain;
 RX MEDLINE=92017079; PubMed=1656157;
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
 RT "Conservation of the sequence of the Alzheimer's disease amyloid
 RT peptide in dog, polar bear and five other mammals by cross-species
 RT polymerase chain reaction analysis."
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).
 CC -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
 CC INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
 CC G(O) (BY SIMILARITY).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -----
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 CC -----
 DR EMBL; X56124; CAA39589.1; -.
 DR EMBL; X56126; CAA39591.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PROSITE; PS00319; A4_EXTRA; PARTIAL.
 DR PROSITE; PS00320; A4_INTRA; PARTIAL.
 KW Glycoprotein; Amyloid; Neurone; Transmembrane.
 FT NON_TER 1 1
 FT CHAIN 7 49 BETA-AMYLOID PROTEIN (POTENTIAL).
 FT DOMAIN <1 34 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 35 58 POTENTIAL.
 FT DOMAIN 59 >59 CYTOPLASMIC (POTENTIAL).
 FT NON_TER 59 59
 SQ SEQUENCE 59 AA; 6414 MW; F43469D488A2E12D CRC64;

Query Match 100.0%; Score 40; DB 1; Length 59;
 Best Local Similarity 100.0%; Pred. No. 0.05;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||

RESULT 6

A4_SAISC

ID_ A4_SAISC STANDARD; PRT; 751 AA.
AC Q95241;
DT 15-DEC-1998 (Rel. 37, Created)
DT 15-DEC-1998 (Rel. 37, Last sequence update)
DT 15-SEP-2003 (Rel. 42, Last annotation update)
DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble
DE APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);
DE Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-
DE CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE secretase C-terminal fragment 50); C31].
GN APP.
OS Saimiri sciureus (Common squirrel monkey).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.
OX NCBI_TaxID=9521;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Kidney, and Liver;
RX MEDLINE=96108492; PubMed=8532114;
RA Levy E., Amorim A., Frangione B., Walker L.C.;
RT "Beta-amyloid precursor protein gene in squirrel monkeys with
RT cerebral amyloid angiopathy."
RL Neurobiol. Aging 16:805-808(1995).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions (By similarity). Can promote transcription activation
CC through binding to APBB1/Tip60 and inhibit Notch signaling through
CC interaction with Numb (By similarity). Couples to apoptosis-
CC inducing pathways such as those mediated by G(0) and JIP (By
CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC Acts as a kinesin I membrane receptor, mediating the axonal
CC transport of beta-secretase and presenilin 1 (By similarity). May
CC be involved in copper homeostasis/oxidative stress through copper
CC ion reduction. In vitro, copper-metallated APP induces neuronal
CC death directly or is potentiated through Cu(II)-mediated low-
CC density lipoprotein oxidation (By similarity). Can regulate
CC neurite outgrowth through binding to components of the
CC extracellular matrix such as heparin and collagen I and IV (By
CC similarity). The splice isoforms that contain the BPTI domain
CC possess protease inhibitor activity (By similarity).
CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC with metal-reducing activity. Bind transient metals such as
CC copper, zinc and iron (By similarity).
CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC peptides, including C31, are potent enhancers of neuronal
CC apoptosis (By similarity).
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC cytoplasmic proteins, including APBB family members, the APBA

family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IBL, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clatherin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. GammaCTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- ALTERNATIVE PRODUCTS:
 Event=Alternative splicing; Named isoforms=2;
 Comment=Additional isoforms seem to exist;
 Name=APP770;
 IsoId=Q95241-1; Sequence=Displayed;
 Name=APP695;
 IsoId=Q95241-2; Sequence=Not described;

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clatherin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the retention of corresponding membrane-anchored C-terminal fragments, C83 and C99. Subsequent processing of C83 by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of C99 releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the cytotoxic C-terminal fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By similarity).

-!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9 results in the production of the neurotoxic C31 peptide and the increased production of beta-amyloid peptides (By similarity).

-!- PTM: N- and O-linked glycosylated (By similarity).

-!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and serine residues is neuron-specific. Phosphorylation can affect APP

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CC      processing, neuronal differentiation and interaction with other
CC      proteins (By similarity).
CC      -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC      zinc, can induce histidine-bridging between beta-amyloid molecules
CC      resulting in beta-amyloid-metal aggregates (By similarity).
CC      Extracellular zinc-binding increases binding of heparin to APP and
CC      inhibits collagen-binding (By similarity).
CC      -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC      -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC      -----
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CC      -----
DR      EMBL; S81024; AAD14347.1; -.
DR      HSSP; P05067; 1AAP.
DR      InterPro; IPR001868; A4_APP.
DR      InterPro; IPR001255; Beta-APP.
DR      InterPro; IPR002223; Kunitz_BPTI.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      Pfam; PF00014; Kunitz_BPTI; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PRINTS; PR00759; BASICPTASE.
DR      ProDom; PD000222; Kunitz_BPTI; 1.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      SMART; SM00131; KU; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
DR      PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR      PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW      Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW      Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW      Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW      Proteoglycan; Amyloid; Alternative splicing.
FT      SIGNAL          1      17      BY SIMILARITY.
FT      CHAIN           18     751      A4 PROTEIN.
FT      CHAIN           18     668      SOLUBLE APP-ALPHA (POTENTIAL).
FT      CHAIN           18     652      SOLUBLE APP-BETA (POTENTIAL).
FT      CHAIN          653     751      C99 (POTENTIAL).
FT      CHAIN          653     694      BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT      CHAIN          653     692      BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT      CHAIN          669     751      C83 (POTENTIAL).
FT      CHAIN          669     694      P3(42) (POTENTIAL).
FT      CHAIN          669     692      P3(40) (POTENTIAL).
FT      CHAIN          693     751      GAMMA-CTF(59) (POTENTIAL).
FT      CHAIN          695     751      GAMMA-CTF(57) (POTENTIAL).
FT      CHAIN          702     751      GAMMA-CTF(50) (POTENTIAL).
FT      CHAIN          721     751      C31 (POTENTIAL).
FT      DOMAIN          18     680      EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM        681     704      POTENTIAL.
FT      DOMAIN          705     751      CYTOPLASMIC (POTENTIAL).
FT      DOMAIN          96     110      HEPARIN-BINDING (BY SIMILARITY).

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| | | | | |
|----|----------|-----|-----|--|
| FT | DOMAIN | 181 | 188 | ZINC-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 291 | 341 | BPTI/KUNITZ INHIBITOR. |
| FT | DOMAIN | 316 | 344 | HEPARIN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 363 | 428 | HEPARIN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 504 | 521 | COLLAGEN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 713 | 732 | INTERACTION WITH G(O)-ALPHA |
| FT | | | | (BY SIMILARITY). |
| FT | DOMAIN | 230 | 260 | ASP/GLU-RICH (ACIDIC). |
| FT | DOMAIN | 274 | 280 | POLY-THR. |
| FT | SITE | 144 | 144 | REQUIRED FOR COPPER(II) REDUCTION |
| FT | | | | (BY SIMILARITY). |
| FT | ACT_SITE | 301 | 302 | REACTIVE BOND. |
| FT | SITE | 652 | 653 | CLEAVAGE (BY BETA-SECRETASE) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 653 | 654 | CLEAVAGE (BY CASPASE-6) (BY SIMILARITY). |
| FT | SITE | 668 | 669 | CLEAVAGE (BY ALPHA-SECRETASE) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 685 | 685 | INVOLVED IN FREE RADICAL PROPAGATION |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 687 | 687 | INVOLVED IN OXIDATIVE REACTIONS |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 692 | 693 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 1) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 694 | 695 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 2) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 701 | 702 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 3) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 705 | 715 | BASOLATERAL SORTING SIGNAL |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 720 | 721 | CLEAVAGE (BY CASPASES-3,-6,-8 OR -9) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 738 | 741 | ENDOCYTOSIS SIGNAL. |
| FT | SITE | 740 | 743 | NPXY MOTIF. |
| FT | METAL | 137 | 137 | COPPER (BY SIMILARITY). |

Query Match 100.0%; Score 40; DB 1; Length 751;
 Best Local Similarity 100.0%; Pred. No. 0.59;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 649 EVKMDAEF 656

RESULT 7

A4_CAVPO

ID A4_CAVPO STANDARD; PRT; 770 AA.
 AC Q60495; Q60496;
 DT 15-SEP-2003 (Rel. 42, Created)
 DT 15-SEP-2003 (Rel. 42, Last sequence update)
 DT 15-SEP-2003 (Rel. 42, Last annotation update)
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
 DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
 DE Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid
 DE protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);
 DE P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-
 DE CTF(57) (Gamma-secretase C-terminal fragment 57); C31].

GN APP.
 OS Cavia porcellus (Guinea pig).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
 OX NCBI_TaxID=10141;
 RN [1]
 RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
 RC TISSUE=Brain, and Liver;
 RX MEDLINE=97236426; PubMed=9116031;
 RA Beck M., Mueller D., Bigl V.;
 RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
 RT alternative splicing.";
 RL Biochim. Biophys. Acta 1351:17-21(1997).
 RN [2]
 RP INTERACTION OF BETA-APP40 WITH APOE.
 RX MEDLINE=98007700; PubMed=9349544;
 RA Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,
 RA Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;
 RT "Isoform-specific effects of apolipoproteins E2, E3, and E4 on
 RT cerebral capillary sequestration and blood-brain barrier transport of
 RT circulating Alzheimer's amyloid beta.";
 RL J. Neurochem. 69:1995-2004(1997).
 RN [3]
 RP PROCESSING.
 RX MEDLINE=20084499; PubMed=10619481;
 RA Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,
 RA Bigl V.;
 RT "Guinea-pig primary cell cultures provide a model to study expression
 RT and amyloidogenic processing of endogenous amyloid precursor
 RT protein.";
 RL Neuroscience 95:243-254(2000).
 RN [4]
 RP GAMMA-SECRETASE PROCESSING.
 RX MEDLINE=20576391; PubMed=11035007;
 RA Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,
 RA Ziani-Cherif C., Onstead L., Sambamurti K.;
 RT "A novel gamma -secretase assay based on detection of the putative
 RT C-terminal fragment-gamma of amyloid beta protein precursor.";
 RL J. Biol. Chem. 276:481-487(2001).
 CC -- FUNCTION: Functions as a cell surface receptor and performs
 CC physiological functions on the surface of neurons relevant to
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in
 CC cell mobility and transcription regulation through protein-protein
 CC interactions (By similarity). Can promote transcription activation
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through
 CC interaction with Numb (By similarity). Couples to apoptosis-
 CC inducing pathways such as those mediated by G(O) and JIP (By
 CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).
 CC Acts as a kinesin I membrane receptor, mediating the axonal
 CC transport of beta-secretase and presenilin 1 (By similarity). May
 CC be involved in copper homeostasis/oxidative stress through copper
 CC ion reduction (By similarity). In vitro, copper-metallated APP
 CC induces neuronal death directly or is potentiated through Cu(II)-
 CC mediated low-density lipoprotein oxidation (By similarity). Can
 CC regulate neurite outgrowth through binding to components of the
 CC extracellular matrix such as heparin and collagen I and IV (By
 CC similarity). The splice isoforms that contain the BPTI domain

possess protease inhibitor activity (By similarity).

-!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators with metal-reducing activity. Bind transient metals such as copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins and apolipoproteins E and J in the CSF and to HDL particles in plasma, inhibiting metal-catalyzed oxidation of lipoproteins.

-!- FUNCTION: Appicans elicit adhesion of neural cells to the extracellular matrix and may regulate neurite outgrowth in the brain (By similarity).

-!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved peptides, including C31, are potent enhancers of neuronal apoptosis (By similarity).

-!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several cytoplasmic proteins, including APBB family members, the APBA family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity). Soluble Abeta40 binds all three isoforms of APOE, in vitro and in vivo. When lipidated, ApoE3 appears to be the preferred amyloid binding isoform, while the apoE4 isoform-beta-APP40 complex is capable of being transported across the blood-brain barrier.

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits (By similarity). During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated) (By similarity). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes (By similarity). Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface (By similarity). APP sorts to the basolateral surface in epithelial cells (By similarity).

-!- ALTERNATIVE PRODUCTS:

Event=Alternative splicing; Named isoforms=2;

Comment=Additional isoforms, missing exons 7,8 and 15, seem to exist. The L-isoforms, missing exon 15, are referred to as appicans;

Name=APP770;

IsoId=Q60495-1; Sequence=Displayed;

Name=APP695;

IsoId=Q60495-2; Sequence=VSP_007221, VSP_007222;

-!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in brain. The longer isoforms containing the BPTI domain are predominantly expressed in peripheral organs such as muscle and liver.

-!- INDUCTION: Increased levels during neuronal differentiation.

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells.

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP

CC require the YENPTY motif for full interaction. These interactions
 CC are independent of phosphorylation on the terminal tyrosine
 CC residue (By similarity). The NPXY site is also involved in
 CC clatherin-mediated endocytosis.
 CC -!- PTM: Proteolytically processed under normal cellular conditions.
 CC Cleavage by alpha-secretase or alternatively by beta-secretase
 CC leads to generation and extracellular release of soluble APP
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the
 CC retention of corresponding membrane-anchored C-terminal fragments,
 CC CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by
 CC gamma-secretase yields P3 peptides. This is the major secretory
 CC pathway and is nonamyloidogenic. Alternatively,
 CC presenilin/nicastrin-mediated gamma-secretase processing of CTF-
 CC beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)
 CC and amyloid-beta 42 (Abeta42), major components of amyloid
 CC plaques, and the corresponding cytotoxic C-terminal fragments
 CC (CTFs).
 CC -!- PTM: Proteolytically cleaved by caspase-3 during neuronal
 CC apoptosis (By similarity).
 CC -!- PTM: N- and O-linked glycosylated. O-linkage of chondroitin
 CC sulfate to the L-APP isoforms produces the APP proteoglycan core
 CC proteins, the appicans (By similarity).
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
 CC serine residues is neuron-specific (By similarity).
 CC Phosphorylation can affect APP processing, neuronal
 CC differentiation and interaction with other proteins.
 CC -!- PTM: Extracellular binding and reduction of copper, results in a
 CC corresponding oxidation of Cys-144 and Cys-158, and the formation
 CC of a disulfide bond (By similarity).
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
 CC zinc, can induce histidine-bridging between beta-amyloid molecules
 CC resulting in beta-amyloid-metal aggregates.
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----
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 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
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 CC -----

DR EMBL; X97631; CAA66230.1; -.
 DR EMBL; X99198; CAA67589.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.

DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW Proteoglycan; Alternative splicing; Amyloid.
FT SIGNAL 1 17 BY SIMILARITY.
FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.
FT CHAIN 18 687 SOLUBLE APP-ALPHA (BY SIMILARITY).
FT CHAIN 18 671 SOLUBLE APP-BETA (BY SIMILARITY).
FT CHAIN 672 770 CTF-ALPHA (BY SIMILARITY).
FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT CHAIN 688 770 CTF-BETA (BY SIMILARITY).
FT CHAIN 688 713 P3(42) (BY SIMILARITY).
FT CHAIN 688 711 P3(40) (BY SIMILARITY).
FT CHAIN 712 770 GAMMA-CTF(59) (BY SIMILARITY).
FT CHAIN 714 770 GAMMA-CTF(57) (BY SIMILARITY).
FT CHAIN 740 770 C31 (BY SIMILARITY).

Query Match 100.0%; Score 40; DB 1; Length 770;
Best Local Similarity 100.0%; Pred. No. 0.61;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
|||||||
Db 668 EVKMDAEF 675

RESULT 8

A4_HUMAN

ID A4_HUMAN STANDARD; PRT; 770 AA.
AC P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q9BT38;
AC Q9UCB6; Q9UQ58;
DT 13-AUG-1987 (Rel. 05, Created)
DT 01-NOV-1991 (Rel. 20, Last sequence update)
DT 15-SEP-2003 (Rel. 42, Last annotation update)
DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease
DE nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-
DE alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42
DE (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);
DE P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)
DE (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-
DE secretase C-terminal fragment 57) (Amyloid intracellular domain 57)
DE (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)
DE (Amyloid intracellular domain 50) (AID(50)); C31].
GN APP OR A4 OR AD1.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A. (ISOFORM APP695).
RC TISSUE=Brain;
RX MEDLINE=87144572; PubMed=2881207;
RA Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,
RA Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;

RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a
 RT cell-surface receptor.";
 RL Nature 325:733-736(1987).
 RN [2]
 RP SEQUENCE FROM N.A. (ISOFORM APP751).
 RC TISSUE=Brain;
 RX MEDLINE=88122639; PubMed=2893289;
 RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,
 RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,
 RA Cordell B.;
 RT "A new A4 amyloid mRNA contains a domain homologous to serine
 RT proteinase inhibitors.";
 RL Nature 331:525-527(1988).
 RN [3]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RX MEDLINE=89128427; PubMed=2783775;
 RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,
 RA Unterbeck A., Beyreuther K., Mueller-Hill B.;
 RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid
 RT is encoded by 16 exons.";
 RL Nucleic Acids Res. 17:517-522(1989).
 RN [4]
 RP SEQUENCE FROM N.A. (ISOFORM APP770).
 RX MEDLINE=90236318; PubMed=2110105;
 RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;
 RT "Genomic organization of the human amyloid beta-protein precursor
 RT gene.";
 RL Gene 87:257-263(1990).
 RN [5]
 RP ERRATUM, AND REVISIONS.
 RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;
 RL Gene 102:291-292(1991).
 RN [6]
 RP SEQUENCE FROM N.A. (ISOFORM L-APP733).
 RC TISSUE=Leukocyte;
 RX MEDLINE=92268136; PubMed=1587857;
 RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,
 RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;
 RT "Identification and differential expression of a novel alternative
 RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in
 RT leukocytes and brain microglial cells.";
 RL J. Biol. Chem. 267:10804-10809(1992).
 RN [7]
 RP SEQUENCE FROM N.A. (ISOFORM APP770).
 RX MEDLINE=97263807; PubMed=9108164;
 RA Hattori M., Tsukahara F., Furuhashi Y., Tanahashi H., Hirose M.,
 RA Saito M., Tsukuni S., Sakaki Y.;
 RT "A novel method for making nested deletions and its application for
 RT sequencing of a 300 kb region of human APP locus.";
 RL Nucleic Acids Res. 25:1802-1808(1997).
 RN [8]
 RP SEQUENCE FROM N.A. (ISOFORM APP305).
 RC TISSUE=Pancreas;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,

RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length
 RT human and mouse cDNA sequences."
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [9]
 RP SEQUENCE OF 1-10 FROM N.A.
 RC TISSUE=Liver;
 RX MEDLINE=89016647; PubMed=3140222;
 RA Schon E.A., Mita S., Sadlock J., Herbert J.;
 RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)
 RT encodes a 95-kDa polypeptide."
 RL Nucleic Acids Res. 16:9351-9351(1988).
 RN [10]
 RP ERRATUM, AND REVISIONS.
 RA Mita S., Sadlock J., Herbert J., Schon E.A.;
 RL Nucleic Acids Res. 16:11402-11402(1988).
 RN [11]
 RP SEQUENCE OF 1-75 FROM N.A.
 RX MEDLINE=89165870; PubMed=2538123;
 RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;
 RT "Characterization of the 5'-end region and the first two exons of the
 RT beta-protein precursor gene."
 RL Biochem. Biophys. Res. Commun. 159:297-304(1989).
 RN [12]
 RP SEQUENCE OF 18-50.
 RC TISSUE=Fibroblast;
 RX MEDLINE=87250462; PubMed=3597385;
 RA van Nostrand W.E., Cunningham D.D.;
 RT "Purification of protease nexin II from human fibroblasts."
 RL J. Biol. Chem. 262:8508-8514(1987).
 RN [13]
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).
 RC TISSUE=Brain;
 RX MEDLINE=89346754; PubMed=2569763;
 RA de Sauvage F., Octave J.N.;
 RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly
 RT secreted protein."
 RL Science 245:651-653(1989).
 RN [14]
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=87231971; PubMed=3035574;
 RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;
 RT "Molecular cloning and characterization of a cDNA encoding the

RT cerebrovascular and the neuritic plaque amyloid peptides.";
 RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).
 RN [15]
 RP SEQUENCE OF 286-366 FROM N.A.
 RX MEDLINE=88122640; PubMed=2893290;
 RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,
 RA Gusella J.F., Neve R.L.;
 RT "Protease inhibitor domain encoded by an amyloid protein precursor
 RT mRNA associated with Alzheimer's disease.";
 RL Nature 331:528-530(1988).
 RN [16]
 RP SEQUENCE OF 287-367 FROM N.A.
 RX MEDLINE=88122641; PubMed=2893291;
 RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;
 RT "Novel precursor of Alzheimer's disease amyloid protein shows
 RT protease inhibitory activity.";
 RL Nature 331:530-532(1988).
 RN [17]
 RP SEQUENCE OF 507-770 FROM N.A.
 RC TISSUE=Brain cortex;
 RX MEDLINE=88124954; PubMed=2893379;
 RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,
 RA Marotta C.A.;
 RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer
 RT disease brain: coding and noncoding regions of the fetal precursor
 RT mRNA are expressed in the cortex.";
 RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).
 RN [18]
 RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.
 RX MEDLINE=96139497; PubMed=8576160;
 RA Behr D., Hesse L., Masters C.L., Multhaup G.;
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and
 RT mapping of the binding sites on APP and collagen type I.";
 RL J. Biol. Chem. 271:1613-1620(1996).
 RN [19]
 RP SEQUENCE OF 656-737 FROM N.A.
 RX MEDLINE=89392030; PubMed=2675837;
 RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,
 RA Little S.P.;
 RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows
 RT similarity to soybean trypsin inhibitor.";
 RL Biochem. Biophys. Res. Commun. 163:1248-1255(1989).
 RN [20]
 RP SEQUENCE OF 672-681.
 RC TISSUE=Brain cortex;
 RX MEDLINE=88035004; PubMed=3312495;
 RA Pardridge W.M., Vinters H.V., Yang J., Eisenberg J., Choi T.B.,
 RA Tourtellotte W.W., Huebner V., Shively J.E.;
 RT "Amyloid angiopathy of Alzheimer's disease: amino acid composition
 RT and partial sequence of a 4,200-dalton peptide isolated from cortical
 RT microvessels.";
 RL J. Neurochem. 49:1394-1401(1987).
 RN [21]
 RP SEQUENCE OF 674-770 FROM N.A.
 RC TISSUE=Brain;
 RX MEDLINE=87120328; PubMed=3810169;
 RA Goldgaber D., Lerman M.I., McBride O.W., Saffiotti U., Gajdusek D.C.;

RT "Characterization and chromosomal localization of a cDNA encoding
RT brain amyloid of Alzheimer's disease.";

Query Match 100.0%; Score 40; DB 1; Length 770;
Best Local Similarity 100.0%; Pred. No. 0.61;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
| | | | | | | |
Db 668 EVKMDAEF 675

RESULT 9

A4_MACFA

ID A4_MACFA STANDARD; PRT; 770 AA.
AC P53601; Q95KN7;
DT 01-OCT-1996 (Rel. 34, Created)
DT 28-FEB-2003 (Rel. 41, Last sequence update)
DT 28-FEB-2003 (Rel. 41, Last annotation update)
DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE secretase C-terminal fragment 50); C31].
GN APP.
OS Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC Cercopithecinae; Macaca.
OX NCBI_TaxID=9541;
RN [1]
RP SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC TISSUE=Cerebellum;
RX MEDLINE=91273117; PubMed=1905108;
RA Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT "Homology of the amyloid beta protein precursor in monkey and human
RT supports a primate model for beta amyloidosis in Alzheimer's
RT disease.";
RL Am. J. Pathol. 138:1423-1435(1991).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions (By similarity). Can promote transcription activation
CC through binding to APBB1/Tip60 and inhibit Notch signaling through
CC interaction with Numb (By similarity). Couples to apoptosis-
CC inducing pathways such as those mediated by G(0) and JIP (By
CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC Acts as a kinesin I membrane receptor, mediating the axonal
CC transport of beta-secretase and presenilin 1 (By similarity). May
CC be involved in copper homeostasis/oxidative stress through copper
CC ion reduction. In vitro, copper-metallated APP induces neuronal
CC death directly or is potentiated through Cu(II)-mediated low-
CC density lipoprotein oxidation (By similarity). Can regulate
CC neurite outgrowth through binding to components of the

CC extracellular matrix such as heparin and collagen I and IV (By
 CC similarity). The splice isoforms that contain the BPTI domain
 CC possess protease inhibitor activity (By similarity).
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
 CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron (By similarity).
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis (By similarity).
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
 CC In vitro, it binds MAPT via the MT-binding domains (By
 CC similarity). Associates with microtubules in the presence of ATP
 CC and in a kinesin-dependent manner (By similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clatherin-coated
 CC pits. During maturation, the immature APP (N-glycosylated in the
 CC endoplasmic reticulum) moves to the Golgi complex where complete
 CC maturation occurs (O-glycosylated and sulfated). After alpha-
 CC secretase cleavage, soluble APP is released into the extracellular
 CC space and the C-terminal is internalized to endosomes and
 CC lysosomes. Some APP accumulates in secretory transport vesicles
 CC leaving the late Golgi compartment and returns to the cell
 CC surface. GammaCTF(59) peptide is located to both the cytoplasm and
 CC nuclei of neurons (By similarity).
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event=Alternative splicing; Named isoforms=2;
 CC Comment=Additional isoforms seem to exist;
 CC Name=APP770;
 CC IsoId=P53601-1; Sequence=Displayed;
 CC Name=APP695;
 CC IsoId=P53601-2; Sequence=VSP_000010, VSP_000011;
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
 CC sorting of membrane proteins to the basolateral surface of
 CC epithelial cells (By similarity).
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
 CC phosphorylated proteins is required for the specific binding of
 CC the PID domain. However additional amino acids either N- or C-
 CC terminal to the NPXY motif are often required for complete
 CC interaction. The PID domain-containing proteins which bind APP
 CC require the YENPTY motif for full interaction. These interactions
 CC are independent of phosphorylation on the terminal tyrosine
 CC residue. The NPXY site is also involved in clatherin-mediated
 CC endocytosis (By similarity).
 CC -!- PTM: Proteolytically processed under normal cellular conditions.
 CC Cleavage by alpha-secretase or alternatively by beta-secretase
 CC leads to generation and extracellular release of soluble APP
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the
 CC retention of corresponding membrane-anchored C-terminal fragments,
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase
 CC yields P3 peptides. This is the major secretory pathway and is
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
 CC gamma-secretase processing of C99 releases the amyloid beta

CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
 CC major components of amyloid plaques, and the cytotoxic C-terminal
 CC fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
 CC similarity).
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
 CC results in the production of the neurotoxic C31 peptide and the
 CC increased production of beta-amyloid peptides (By similarity).
 CC -!- PTM: N- and O-linked glycosylated (By similarity).
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
 CC serine residues is neuron-specific. Phosphorylation can affect APP
 CC processing, neuronal differentiation and interaction with other
 CC proteins (By similarity).
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
 CC zinc, can induce histidine-bridging between beta-amyloid molecules
 CC resulting in beta-amyloid-metal aggregates (By similarity).
 CC Extracellular zinc-binding increases binding of heparin to APP and
 CC inhibits collagen-binding (By similarity).
 CC -!- SIMILARITY: BELONGS TO THE APP FAMILY.
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
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 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL; M58727; AAA36829.1; -.
 DR EMBL; M58726; AAA36828.1; -.
 DR HSSP; P05067; 1AAP.
 DR InterPro; IPR001868; A4_APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
 KW Proteoglycan; Alternative splicing; Amyloid.
 FT SIGNAL 1 17 BY SIMILARITY.
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).
 FT CHAIN 672 770 C99 (POTENTIAL).
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (POTENTIAL).
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (POTENTIAL).
 FT CHAIN 688 770 C83 (POTENTIAL).

| | | | | |
|----|----------|-----|-----|--|
| FT | CHAIN | 688 | 713 | P3(42) (POTENTIAL). |
| FT | CHAIN | 688 | 711 | P3(40) (POTENTIAL). |
| FT | CHAIN | 712 | 770 | GAMMA-CTF(59) (POTENTIAL). |
| FT | CHAIN | 714 | 770 | GAMMA-CTF(57) (POTENTIAL). |
| FT | CHAIN | 721 | 770 | GAMMA-CTF(50) (POTENTIAL). |
| FT | CHAIN | 740 | 770 | C31 (POTENTIAL). |
| FT | DOMAIN | 18 | 699 | EXTRACELLULAR (POTENTIAL). |
| FT | TRANSMEM | 700 | 723 | POTENTIAL. |
| FT | DOMAIN | 724 | 770 | CYTOPLASMIC (POTENTIAL). |
| FT | DOMAIN | 96 | 110 | HEPARIN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 181 | 188 | ZINC-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 291 | 341 | BPTI/KUNITZ INHIBITOR. |
| FT | DOMAIN | 391 | 423 | HEPARIN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 491 | 522 | HEPARIN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 523 | 540 | COLLAGEN-BINDING (BY SIMILARITY). |
| FT | DOMAIN | 732 | 751 | INTERACTION WITH G(O)-ALPHA |
| FT | | | | (BY SIMILARITY). |
| FT | DOMAIN | 230 | 260 | ASP/GLU-RICH (ACIDIC). |
| FT | DOMAIN | 274 | 280 | POLY-THR. |
| FT | SITE | 144 | 144 | REQUIRED FOR COPPER(II) REDUCTION |
| FT | | | | (BY SIMILARITY). |
| FT | ACT_SITE | 301 | 302 | REACTIVE BOND (BY SIMILARITY). |
| FT | SITE | 671 | 672 | CLEAVAGE (BY BETA-SECRETASE) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 672 | 673 | CLEAVAGE (BY CASPASE-6) (BY SIMILARITY). |
| FT | SITE | 687 | 688 | CLEAVAGE (BY ALPHA-SECRETASE) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 704 | 704 | IMPLICATED IN FREE RADICAL PROPAGATION |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 706 | 706 | INVOLVED IN OXIDATIVE REACTIONS |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 711 | 712 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 1) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 713 | 714 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 2) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 720 | 721 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 3) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 724 | 734 | BASOLATERAL SORTING SIGNAL |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 739 | 740 | CLEAVAGE (BY CASPASES-3,-6,-8 OR -9) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 757 | 760 | ENDOCYTOSIS SIGNAL. |
| FT | SITE | 759 | 762 | NPXY MOTIF. |

Query Match 100.0%; Score 40; DB 1; Length 770;

Best Local Similarity 100.0%; Pred. No. 0.61;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 668 EVKMDAEF 675

RESULT 10

A4_MOUSE

ID A4_MOUSE STANDARD; PRT; 770 AA.

AC P12023; P97487; P97942; Q99K32;

DT 01-OCT-1989 (Rel. 12, Created)
 DT 15-SEP-2003 (Rel. 42, Last sequence update)
 DT 15-SEP-2003 (Rel. 42, Last annotation update)
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
 DE amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:
 DE Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99
 DE (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein
 DE 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase
 DE C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))
 DE (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)
 DE (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)
 DE (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain
 DE 50) (AID(50)); C31].
 GN APP.
 OS Mus musculus (Mouse).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 OX NCBI_TaxID=10090;
 RN [1]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=88106489; PubMed=3322280;
 RA Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;
 RT "Complementary DNA for the mouse homolog of the human amyloid beta
 RT protein precursor.";
 RL Biochem. Biophys. Res. Commun. 149:665-671(1987).
 RN [2]
 RP REVISIONS.
 RA Yamada T.;
 RL Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.
 RN [3]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC STRAIN=BALB/c; TISSUE=Brain;
 RX MEDLINE=92096458; PubMed=1756177;
 RA de Strooper B., van Leuven F., van den Berghe H.;
 RT "The amyloid beta protein precursor or proteinase nexin II from mouse
 RT is closer related to its human homolog than previously reported.";
 RL Biochim. Biophys. Acta 1129:141-143(1991).
 RN [4]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC STRAIN=SAMP8; TISSUE=Hippocampus;
 RX PubMed=11235921;
 RA Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,
 RA Alvarez J., Morley J.E.;
 RT "Molecular cloning, expression, and regulation of hippocampal amyloid
 RT precursor protein of senescence accelerated mouse (SAMP8).";
 RL Biochem. Cell Biol. 79:57-67(2001).
 RN [5]
 RP SEQUENCE OF 1-19 FROM N.A.
 RX MEDLINE=92209998; PubMed=1555768;
 RA Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,
 RA Sakai Y.;
 RT "Positive and negative regulatory elements for the expression of the
 RT Alzheimer's disease amyloid precursor-encoding gene in mouse.";
 RL Gene 112:189-195(1992).
 RN [6]
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).

RC TISSUE=Breast tumor;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length human
 RT and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [7]
 RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.
 RC TISSUE=Brain, and Kidney;
 RX MEDLINE=89149813; PubMed=2493250;
 RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;
 RT "Structure and expression of the alternatively-spliced forms of mRNA
 RT for the mouse homolog of Alzheimer's disease amyloid beta protein
 RT precursor.";
 RL Biochem. Biophys. Res. Commun. 158:906-912(1989).
 RN [8]
 RP SEQUENCE OF 289-364 FROM N.A.
 RC STRAIN=CD-1; TISSUE=Placenta;
 RX MEDLINE=89345111; PubMed=2569710;
 RA Fukuchi K., Martin G.M., Deeb S.S.;
 RT "Sequence of the protease inhibitor domain of the A4 amyloid protein
 RT precursor of Mus domesticus.";
 RL Nucleic Acids Res. 17:5396-5396(1989).
 RN [9]
 RP SEQUENCE OF 656-737 FROM N.A.
 RC STRAIN=129/Sv;
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
 RA Loring J.F., Goate A.M.;
 RT "Introduction of six mutations into the mouse genome using 'Hit and
 RT Run' gene-targeting: introduction of familial Alzheimer's disease
 RT mutations into the mouse amyloid precursor protein gene and
 RT humanization of the A-beta fragment.";
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
 RN [10]
 RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.
 RX PubMed=8510506;
 RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;
 RT "Regional distribution of the alternatively spliced isoforms of beta
 RT APP RNA transcript in the brain of normal, heterozygous and
 RT homozygous weaver mutant mice as revealed by in situ hybridization
 RT histochemistry.";

RL Brain Res. Mol. Brain Res. 17:340-346(1993).
 RN [11]
 RP INTERACTION WITH KNS2.
 RX PubMed=11144355;
 RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;
 RT "Axonal transport of amyloid precursor protein is mediated by direct
 RT binding to the kinesin light chain subunit of kinesin-I."
 RL Neuron 28:449-459(2000).
 RN [12]
 RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;
 RP THR-743; TYR-757; ASN-759 AND TYR-762.
 RX MEDLINE=21408156; PubMed=11517249;
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,
 RA Kyriakis J.M., Nishimoto I.;
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1
 RT scaffolds Alzheimer's amyloid precursor protein with JNK."
 RL J. Neurosci. 21:6597-6607(2001).
 RN [13]
 RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.
 RX MEDLINE=22028091; PubMed=11912189;
 RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;
 RT "Interaction of Alzheimer's beta-amyloid precursor family proteins
 RT with scaffold proteins of the JNK signaling cascade."
 RL J. Biol. Chem. 277:20070-20078(2002).
 RN [14]
 RP INTERACTION OF CTF PEPTIDES WITH NUMB.
 RX PubMed=12011466;
 RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,
 RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;
 RT "The gamma-secretase-generated intracellular domain of beta-amyloid
 RT precursor protein binds Numb and inhibits Notch signaling."
 RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).
 RN [15]
 RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.
 RX PubMed=11553691;
 RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;
 RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by
 RT gamma-secretase is rapidly degraded but distributes partially in a
 RT nuclear fraction of neurones in culture."
 RL J. Neurochem. 78:1168-1178(2001).
 CC -!- FUNCTION: Functions as a cell surface receptor and performs
 CC physiological functions on the surface of neurons relevant to
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in
 CC cell mobility and transcription regulation through protein-protein
 CC interactions. Can promote transcription activation through binding
 CC to APBB1/Tip60 and inhibit Notch signaling through interaction
 CC with Numb. Couples to apoptosis-inducing pathways such as those
 CC mediated by G(0) and JIP. Inhibits G(0) alpha ATPase activity (By
 CC similarity). Acts as a kinesin I membrane receptor, mediating the
 CC axonal transport of beta-secretase and presenilin 1. May be
 CC involved in copper homeostasis/oxidative stress through copper ion
 CC reduction. Can regulate neurite outgrowth through binding to
 CC components of the extracellular matrix such as heparin and
 CC collagen I and IV (By similarity). The splice isoforms that
 CC contain the BPTI domain possess protease inhibitor activity (By
 CC similarity).

CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
 CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
 CC only weakly transient metals and have little reducing activity due
 CC to substitutions of transient metal chelating residues. Beta-APP42
 CC may activate mononuclear phagocytes in the brain and elicit
 CC inflammatory responses. Promotes both tau aggregation and TPK II-
 CC mediated phosphorylation (By similarity).
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis.
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits
 CC its serine phosphorylation. Also interacts with GPCR-like protein
 CC BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via
 CC BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the
 CC MT-binding domains (By similarity). Associates with microtubules
 CC in the presence of ATP and in a kinesin-dependent manner (By
 CC similarity). Interacts, through a C-terminal domain, with GNAO1
 CC (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal
 CC neurons (By similarity). Beta-amyloid associates with HADH2 (By
 CC similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clatherin-coated
 CC pits. During maturation, the immature APP (N-glycosylated in the
 CC endoplasmic reticulum) moves to the Golgi complex where complete

Query Match 100.0%; Score 40; DB 1; Length 770;
 Best Local Similarity 100.0%; Pred. No. 0.61;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||||
 Db 668 EVKMDAEF 675

RESULT 11

A4_PIG
 ID A4_PIG STANDARD; PRT; 770 AA.
 AC P79307; Q29023; Q9TUI0;
 DT 01-NOV-1997 (Rel. 35, Created)
 DT 15-SEP-2003 (Rel. 42, Last sequence update)
 DT 15-SEP-2003 (Rel. 42, Last annotation update)
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
 DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
 DE Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
 DE APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
 DE Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
 DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
 DE secretase C-terminal fragment 50); C31].
 OS Sus scrofa (Pig).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
 OX NCBI_TaxID=9823;
 RN [1]
 RP SEQUENCE FROM N.A.

RA Kimura A., Takahashi T.;
 RT "Amyloid precursor protein 770.";
 RL Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
 RN [2]
 RP SEQUENCE OF 1-136 FROM N.A.
 RC TISSUE=Small intestine;
 RA Winteroe A.K., Fredholm M.;
 RT "Evaluation and characterization of a porcine small intestine cDNA
 RT library.";
 RL Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
 RN [3]
 RP SEQUENCE OF 667-723 FROM N.A.
 RC TISSUE=Brain;
 RX MEDLINE=92017079; PubMed=1656157;
 RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
 RT "Conservation of the sequence of the Alzheimer's disease amyloid
 RT peptide in dog, polar bear and five other mammals by cross-species
 RT polymerase chain reaction analysis.";
 RL Brain Res. Mol. Brain Res. 10:299-305(1991).
 CC -!- FUNCTION: Functions as a cell surface receptor and performs
 CC physiological functions on the surface of neurons relevant to
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in
 CC cell mobility and transcription regulation through protein-protein
 CC interactions (By similarity). Can promote transcription activation
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through
 CC interaction with Numb (By similarity). Couples to apoptosis-
 CC inducing pathways such as those mediated by G(O) and JIP (By
 CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).
 CC Acts as a kinesin I membrane receptor, mediating the axonal
 CC transport of beta-secretase and presenilin 1 (By similarity). May
 CC be involved in copper homeostasis/oxidative stress through copper
 CC ion reduction (By similarity). In vitro, copper-metallated APP
 CC induces neuronal death directly or is potentiated through Cu(II)-
 CC mediated low-density lipoprotein oxidation (By similarity). Can
 CC regulate neurite outgrowth through binding to components of the
 CC extracellular matrix such as heparin and collagen I and IV (By
 CC similarity).
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
 CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron (By similarity).
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis (By similarity).
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
 CC In vitro, it binds MAPT via the MT-binding domains (By
 CC similarity). Associates with microtubules in the presence of ATP
 CC and in a kinesin-dependent manner (By similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clatherin-coated
 CC pits. During maturation, the immature APP (N-glycosylated in the
 CC endoplasmic reticulum) moves to the Golgi complex where complete
 CC maturation occurs (O-glycosylated and sulfated). After alpha-

secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. GammaCTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clatherin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the retention of corresponding membrane-anchored C-terminal fragments, C83 and C99. Subsequent processing of C83 by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of C99 releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the cytotoxic C-terminal fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By similarity).

-!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9 results in the production of the neurotoxic C31 peptide and the increased production of beta-amyloid peptides (By similarity).

-!- PTM: N- and O-linked glycosylated (By similarity).

-!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and serine residues is neuron-specific. Phosphorylation can affect APP processing, neuronal differentiation and interaction with other proteins (By similarity).

-!- PTM: Extracellular binding and reduction of copper, results in a corresponding oxidation of Cys-144 and Cys-158, and the formation of a disulfide bond (By similarity).

-!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and zinc, can induce histidine-bridging between beta-amyloid molecules resulting in beta-amyloid-metal aggregates (By similarity). Extracellular zinc-binding increases binding of heparin to APP and inhibits collagen-binding (By similarity).

-!- SIMILARITY: BELONGS TO THE APP FAMILY.

-!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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CC -----

DR EMBL; AB032550; BAA84580.1; -.
DR EMBL; Z84022; CAB06313.1; -.
DR EMBL; X56127; CAA39592.1; -.
DR HSSP; P05067; 1AAP.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR InterPro; IPR001255; Beta-APP.
DR InterPro; IPR002223; Kunitz_BPTI.
DR Pfam; PF02177; A4_EXTRA; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR PRINTS; PR00759; BASICPTASE.
DR ProDom; PD000222; Kunitz_BPTI; 1.
DR SMART; SM00006; A4_EXTRA; 1.
DR SMART; SM00131; KU; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW Amyloid.
FT SIGNAL 1 17 BY SIMILARITY.
FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.
FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).
FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).
FT CHAIN 672 770 C99 (BY SIMILARITY).
FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT CHAIN 688 770 C83 (BY SIMILARITY).
FT CHAIN 688 713 P3(42) (BY SIMILARITY).
FT CHAIN 688 711 P3(40) (BY SIMILARITY).
FT CHAIN 712 770 GAMMA-CTF(59).
FT CHAIN 714 770 GAMMA-CTF(57).
FT CHAIN 721 770 GAMMA-CTF(50) (BY SIMILARITY).
FT CHAIN 740 770 C31 (DURING APOPTOSIS) (BY SIMILARITY).
FT DOMAIN 18 699 EXTRACELLULAR (POTENTIAL).
FT TRANSMEM 700 723 POTENTIAL.
FT DOMAIN 724 770 CYTOPLASMIC (POTENTIAL).
FT DOMAIN 96 110 HEPARIN-BINDING (BY SIMILARITY).
FT DOMAIN 135 155 COPPER-BINDING (BY SIMILARITY).
FT DOMAIN 181 188 ZINC-BINDING (BY SIMILARITY).
FT DOMAIN 291 341 BPTI/KUNITZ INHIBITOR.
FT DOMAIN 391 423 HEPARIN-BINDING (BY SIMILARITY).
FT DOMAIN 491 522 HEPARIN-BINDING (BY SIMILARITY).
FT DOMAIN 523 540 COLLAGEN-BINDING (BY SIMILARITY).
FT DOMAIN 732 751 INTERACTION WITH G(O)-ALPHA (BY
FT SIMILARITY).
FT DOMAIN 230 260 ASP/GLU-RICH (ACIDIC).
FT DOMAIN 274 280 POLY-THR.
FT SITE 144 144 REQUIRED FOR COPPER(II) REDUCTION
FT (BY SIMILARITY).
FT ACT_SITE 301 302 REACTIVE BOND (BY SIMILARITY).
FT SITE 671 672 CLEAVAGE (BY BETA-SECRETASE)
FT (BY SIMILARITY).

| | | | | |
|----|------|-----|-----|--|
| FT | SITE | 672 | 673 | CLEAVAGE (BY CASPASE-6) (BY SIMILARITY). |
| FT | SITE | 687 | 688 | CLEAVAGE (BY ALPHA-SECRETASE) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 704 | 704 | IMPLICATED IN FREE RADICAL PROPAGATION |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 706 | 706 | INVOLVED IN OXIDATIVE REACTIONS |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 711 | 712 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 1) |
| FT | | | | (BY SIMILARITY). |
| FT | SITE | 713 | 714 | CLEAVAGE (BY GAMMA-SECRETASE; SITE 2) |
| FT | | | | (BY SIMILARITY). |

Query Match 100.0%; Score 40; DB 1; Length 770;
 Best Local Similarity 100.0%; Pred. No. 0.61;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 668 EVKMDAEF 675

RESULT 12

A4_RAT

ID A4_RAT STANDARD; PRT; 770 AA.
 AC P08592;
 DT 01-AUG-1988 (Rel. 08, Created)
 DT 01-DEC-1992 (Rel. 24, Last sequence update)
 DT 15-SEP-2003 (Rel. 42, Last annotation update)
 DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
 DE protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble
 DE APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-
 DE amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);
 DE C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal
 DE fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);
 DE Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].
 GN APP.
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_TaxID=10116;
 RN [1]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=88312583; PubMed=2900758;
 RA Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,
 RA Seeburg P.H.;
 RT "Alzheimer's disease amyloidogenic glycoprotein: expression pattern
 RT in rat brain suggests a role in cell contact."
 RL EMBO J. 7:1365-1370(1988).
 RN [2]
 RP SEQUENCE OF 289-364 FROM N.A.
 RC TISSUE=Liver;
 RX MEDLINE=89183625; PubMed=2648331;
 RA Kang J., Mueller-Hill B.;
 RT "The sequence of the two extra exons in rat preA4."
 RL Nucleic Acids Res. 17:2130-2130(1989).
 RN [3]

RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.
 RX PubMed=11483588;
 RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;
 RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein
 RT family resembling gamma-secretase-like cleavage of Notch.";
 RL J. Biol. Chem. 276:35235-35238(2001).
 RN [4]
 RP ALTERNATIVE SPLICING.
 RX PubMed=8624099;
 RA Sandbrink R., Masters C.L., Beyreuther K.;
 RT "APP gene family. Alternative splicing generates functionally related
 RT isoforms.";
 RL Ann. N.Y. Acad. Sci. 777:281-287(1996).
 RN [5]
 RP TISSUE SPECIFICITY OF APPICAN.
 RX PubMed=7744833;
 RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,
 RA Mytilineou C., Margolis R.U., Robakis N.K.;
 RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in
 RT brain and is produced by astrocytes but not by neurons in primary
 RT neural cultures.";
 RL J. Biol. Chem. 270:11839-11844(1995).
 RN [6]
 RP TISSUE SPECIFICITY OF ISOFORMS.
 RX PubMed=8996834;
 RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;
 RT "Expression of the APP gene family in brain cells, brain development
 RT and aging.";
 RL Gerontology 43:119-131(1997).
 RN [7]
 RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND
 RP TYR-762.
 RX PubMed=9930726;
 RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,
 RA Suzuki T., Nairn A.C., Greengard P.;
 RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the
 RT Alzheimer's amyloid precursor protein.";
 RL J. Neurochem. 72:549-556(1999).
 RN [8]
 RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF HIS-732 AND HIS-733.
 RX PubMed=10024358;
 RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouilliot C.,
 RA Valenza C., Prochiantz A., Allinquant B.;
 RT "The amyloid precursor protein interacts with Go heterotrimeric
 RT protein within a cell compartment specialized in signal
 RT transduction.";
 RL J. Neurosci. 19:1717-1727(1999).
 RN [9]
 RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.
 RX MEDLINE=95256193; PubMed=7737970;
 RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;
 RT "The chondroitin sulfate attachment site of appican is formed by
 RT splicing out exon 15 of the amyloid precursor gene.";
 RL J. Biol. Chem. 270:10388-10391(1995).
 RN [10]
 RP BETA-AMYLOID METAL-BINDING.
 RX PubMed=10386999;

RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,
 RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,
 RA Bush A.I.;
 RT "The A beta peptide of Alzheimer's disease directly produces hydrogen
 RT peroxide through metal ion reduction.";
 RL Biochemistry 38:7609-7616(1999).
 RN [11]
 RP BETA-AMYLOID ZINC BINDING.
 RX MEDLINE=99343552; PubMed=10413512;
 RA Liu S.T., Howlett G., Barrow C.J.;
 RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation
 RT of the A beta peptide of Alzheimer's disease.";
 RL Biochemistry 38:9373-9378(1999).
 RN [12]
 RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF
 RP GLY-704.
 RX PubMed=11959460;
 RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;
 RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-
 RT peptide 1-42-associated oxidative stress and neurotoxicity.";
 RL Biochim. Biophys. Acta 1586:190-198(2001).
 RN [13]
 RP PHOSPHORYLATION.
 RX PubMed=9085254;
 RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,
 RA Greengard P., Suzuki T.;
 RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is
 RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and
 RT cultured cells.";
 RL Mol. Med. 3:111-123(1997).
 RN [14]
 RP PHOSPHORYLATION ON SER-730.
 RX PubMed=10329382;
 RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,
 RA Greengard P., Nairn A.C., Suzuki T.;
 RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid
 RT precursor protein at Ser655 by a novel protein kinase.";
 RL Biochem. Biophys. Res. Commun. 258:300-305(1999).
 RN [15]
 RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF
 RP THR-743.
 RX MEDLINE=99274744; PubMed=10341243;
 RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,
 RA Kirino Y., Greengard P., Suzuki T.;
 RT "Role of phosphorylation of Alzheimer's amyloid precursor protein
 RT during neuronal differentiation.";
 RL J. Neurosci. 19:4421-4427(1999).
 RN [16]
 RP PHOSPHORYLATION ON THR-743.
 RX PubMed=10936190;
 RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,
 RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;
 RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor
 RT protein by cyclin-dependent kinase 5.";
 RL J. Neurochem. 75:1085-1091(2000).
 RN [17]
 RP CARBOHYDRATE STRUCTURE OF APPICAN.

RX PubMed=11479316;
RA Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,
RA Sugahara K., Robakis N.K.;
RT "Appican, the proteoglycan form of the amyloid precursor protein,
RT contains chondroitin sulfate E in the repeating disaccharide region
RT and 4-O-sulfated galactose in the linkage region.";
RL J. Biol. Chem. 276:37155-37160(2001).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions (By similarity). Can promote transcription activation
CC through binding to APBB1/Tip60 and inhibit Notch signaling through
CC interaction with Numb (By similarity). Couples to apoptosis-
CC inducing pathways such as those mediated by G(O) and JIP. Inhibits
CC G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,
CC mediating the axonal transport of beta-secretase and presenilin 1
CC (By similarity). May be involved in copper homeostasis/oxidative
CC stress through copper ion reduction. Can regulate neurite
CC outgrowth through binding to components of the extracellular
CC matrix such as heparin and collagen I and IV (By similarity). The
CC splice isoforms that contain the BPTI domain possess protease
CC inhibitor activity (By similarity).
CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC with metal-reducing activity. Bind transient metals such as
CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC only weakly transient metals and have little reducing activity due
CC to substitutions of transient metal chelating residues. Beta-APP42
CC may activate mononuclear phagocytes in the brain and elicit
CC inflammatory responses. Promotes both tau aggregation and TPK II-
CC mediated phosphorylation (By similarity).
CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC extracellular matrix and may regulate neurite outgrowth in the
CC brain.
CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC peptides, including C31, are potent enhancers of neuronal
CC apoptosis (By similarity).
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC cytoplasmic proteins, including APBB family members, the APBA
CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding
CC to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.
CC In vitro, it binds MAPT via the MT-binding domains (By
CC similarity). Associates with microtubules in the presence of ATP
CC and in a kinesin-dependent manner (By similarity). Interacts,
CC through a C-terminal domain, with GNAO1. Amyloid beta-42 binds
CC CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid
CC associates with HADH2 (By similarity).
CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC protein that rapidly becomes internalized via clatherin-coated
CC pits. During maturation, the immature APP (N-glycosylated in the

Query Match 100.0%; Score 40; DB 1; Length 770;
Best Local Similarity 100.0%; Pred. No. 0.61;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||||
 Db 668 EVKMDAEF 675

RESULT 13

BCPA_CHLLT

ID BCPA_CHLLT STANDARD; PRT; 354 AA.
 AC Q46135;
 DT 15-JUL-1998 (Rel. 36, Created)
 DT 15-JUL-1998 (Rel. 36, Last sequence update)
 DT 15-SEP-2003 (Rel. 42, Last annotation update)
 DE Bacteriochlorophyll A protein (BChl a protein) (BCP) (Fenna-Matthews-
 DE Olson protein) (FMO-protein) (Fragment).
 GN FMOA.
 OS Chlorobium limicola f.sp. thiosulfatophilum.
 OC Bacteria; Chlorobi; Chlorobia; Chlorobiales; Chlorobiaceae;
 OC Chlorobium.
 OX NCBI_TaxID=115852;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=95352646; PubMed=7626630;
 RA Hager-Braun C., Xie D.L., Jarosch U., Herold E., Buttner M.,
 RA Zimmermann R., Deutzmann R., Hauska G., Nelson N.;
 RT "Stable photobleaching of P840 in Chlorobium reaction center
 RT preparations: presence of the 42-kDa bacteriochlorophyll a protein
 RT and a 17-kDa polypeptide."
 RL Biochemistry 34:9617-9624(1995).
 CC -!- FUNCTION: INTERMEDIARY IN THE TRANSFER OF EXCITATION ENERGY FROM
 CC THE CHLOROPHYLL TO THE REACTION CENTERS.
 CC -!- SUBUNIT: HOMOTRIMER. EACH SUBUNIT CONTAINS 7 MOLECULES OF
 CC BACTERIOCHLOROPHYLL A.

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DR EMBL; X83529; CAA58510.1; -.
 DR PIR; S51143; S51143.
 DR HSSP; Q46393; 1KSA.
 DR InterPro; IPR003426; BChl_A.
 DR Pfam; PF02327; BChl_A; 1.
 DR ProDom; PD041784; BChl_A; 1.
 KW Electron transport; Photosynthesis; Reaction center; Magnesium;
 KW Bacteriochlorophyll.
 FT NON_TER 1 1
 FT METAL 99 99 MAGNESIUM (BACTERIOCHLOROPHYLL A 1 AXIAL
 FT LIGAND) (BY SIMILARITY).
 FT METAL 134 134 MAGNESIUM (BACTERIOCHLOROPHYLL A 6 AXIAL
 FT LIGAND) (BY SIMILARITY).
 FT METAL 278 278 MAGNESIUM (BACTERIOCHLOROPHYLL A 4 AXIAL
 FT LIGAND) (BY SIMILARITY).
 FT METAL 285 285 MAGNESIUM (BACTERIOCHLOROPHYLL A 7 AXIAL

FT LIGAND) (BY SIMILARITY).
 FT METAL 286 286 MAGNESIUM (BACTERIOCHLOROPHYLL A 3 AXIAL
 FT LIGAND) (BY SIMILARITY).
 SQ SEQUENCE 354 AA; 39243 MW; F4D4D565BDDCDB1B CRC64;

Query Match 80.0%; Score 32; DB 1; Length 354;
 Best Local Similarity 75.0%; Pred. No. 15;
 Matches 6; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||:| ||
 Db 254 EVKVDGEF 261

RESULT 14

BCPA_CHLTE

ID BCPA_CHLTE STANDARD; PRT; 365 AA.
 AC Q46393;
 DT 15-JUL-1998 (Rel. 36, Created)
 DT 15-JUL-1998 (Rel. 36, Last sequence update)
 DT 15-SEP-2003 (Rel. 42, Last annotation update)
 DE Bacteriochlorophyll A protein (Bchl a protein) (BCP) (Fenna-Matthews-
 DE Olson protein) (FMO-protein).
 GN FMOA OR CT1499.
 OS Chlorobium tepidum.
 OC Bacteria; Chlorobi; Chlorobia; Chlorobiales; Chlorobiaceae;
 OC Chlorobium.
 OX NCBI_TaxID=1097;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Dracheva S., Williams J.A.C., Blankenship R.E.;
 RT "Cloning and sequencing of the FMO-protein gene from Chlorobium
 RT tepidum.";
 RL (In) Murata N. (eds.);
 RL Research in photosynthesis, pp.2:53-56, Kluwer Academic Publishers,
 RL Dordrecht (1992).
 RN [2]
 RP SEQUENCE FROM N.A.
 RC STRAIN=TLS / ATCC 49652 / DSM 12025;
 RX MEDLINE=22103685; PubMed=12093901;
 RA Eisen J.A., Nelson K.E., Paulsen I.T., Heidelberg J.F., Wu M.,
 RA Dodson R.J., Deboy R., Gwinn M.L., Nelson W.C., Haft D.H.,
 RA Hickey E.K., Peterson J.D., Durkin A.S., Kolonay J.L., Yang F.,
 RA Holt I., Umayam L.A., Mason T., Brenner M., Shea T.P., Parksey D.,
 RA Nierman W.C., Feldblyum T.V., Hansen C.L., Craven M.B., Radune D.,
 RA Vamathevan J., Khouri H., White O., Gruber T.M., Ketchum K.A.,
 RA Venter J.C., Tettelin H., Bryant D.A., Fraser C.M.;
 RT "The complete genome sequence of Chlorobium tepidum TLS, a
 RT photosynthetic, anaerobic, green-sulfur bacterium.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:9509-9514(2002).
 RN [3]
 RP X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS).
 RX MEDLINE=97415773; PubMed=9268671;
 RA Li Y.F., Zhou W., Blankenship R.E., Allen J.P.;
 RT "Crystal structure of the bacteriochlorophyll a protein from
 RT Chlorobium tepidum.";
 RL J. Mol. Biol. 271:456-471(1997).

CC -!- FUNCTION: INTERMEDIARY IN THE TRANSFER OF EXCITATION ENERGY FROM
 CC THE CHLOROPHYLL TO THE REACTION CENTERS.
 CC -!- SUBUNIT: HOMOTRIMER. EACH SUBUNIT CONTAINS 7 MOLECULES OF
 CC BACTERIOCHLOROPHYLL A.

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 CC -----

DR EMBL; L13700; AAA23111.1; -.
 DR EMBL; AE012906; AAM72726.1; -.
 DR PDB; 1KSA; 25-FEB-98.
 DR PDB; 1M50; 25-FEB-03.
 DR TIGR; CT1499; -.

DR InterPro; IPR003426; BChl_A.
 DR Pfam; PF02327; BChl_A; 1.
 DR ProDom; PD041784; BChl_A; 1.

KW Electron transport; Photosynthesis; Reaction center; Magnesium;
 KW 3D-structure; Bacteriochlorophyll; Complete proteome.

| | | | | |
|----|----------|-----|-----|--|
| FT | INIT_MET | 0 | 0 | BY SIMILARITY. |
| FT | METAL | 110 | 110 | MAGNESIUM (BACTERIOCHLOROPHYLL A 1 AXIAL |
| FT | | | | LIGAND). |
| FT | METAL | 145 | 145 | MAGNESIUM (BACTERIOCHLOROPHYLL A 6 AXIAL |
| FT | | | | LIGAND). |
| FT | METAL | 289 | 289 | MAGNESIUM (BACTERIOCHLOROPHYLL A 4 AXIAL |
| FT | | | | LIGAND). |
| FT | METAL | 296 | 296 | MAGNESIUM (BACTERIOCHLOROPHYLL A 7 AXIAL |
| FT | | | | LIGAND). |
| FT | METAL | 297 | 297 | MAGNESIUM (BACTERIOCHLOROPHYLL A 3 AXIAL |
| FT | | | | LIGAND). |
| FT | STRAND | 11 | 19 | |
| FT | STRAND | 27 | 33 | |
| FT | STRAND | 46 | 49 | |
| FT | STRAND | 51 | 55 | |
| FT | STRAND | 65 | 68 | |
| FT | STRAND | 71 | 74 | |
| FT | TURN | 75 | 76 | |
| FT | STRAND | 77 | 78 | |
| FT | STRAND | 81 | 86 | |
| FT | STRAND | 89 | 91 | |
| FT | TURN | 92 | 93 | |
| FT | STRAND | 94 | 95 | |
| FT | STRAND | 99 | 105 | |
| FT | TURN | 106 | 107 | |
| FT | STRAND | 108 | 109 | |
| FT | STRAND | 112 | 122 | |
| FT | HELIX | 129 | 132 | |
| FT | STRAND | 141 | 152 | |
| FT | HELIX | 156 | 167 | |
| FT | TURN | 168 | 168 | |
| FT | HELIX | 174 | 176 | |
| FT | TURN | 177 | 179 | |
| FT | HELIX | 180 | 183 | |

| | | | |
|----|----------|---|-----|
| FT | TURN | 186 | 187 |
| FT | HELIX | 188 | 194 |
| FT | TURN | 195 | 195 |
| FT | STRAND | 204 | 210 |
| FT | TURN | 213 | 214 |
| FT | STRAND | 217 | 222 |
| FT | STRAND | 224 | 228 |
| FT | HELIX | 233 | 236 |
| FT | TURN | 237 | 238 |
| FT | HELIX | 239 | 241 |
| FT | TURN | 245 | 246 |
| FT | STRAND | 251 | 260 |
| FT | TURN | 261 | 262 |
| FT | STRAND | 263 | 264 |
| FT | STRAND | 266 | 269 |
| FT | STRAND | 272 | 272 |
| FT | TURN | 280 | 281 |
| FT | STRAND | 284 | 284 |
| FT | HELIX | 291 | 297 |
| FT | TURN | 298 | 300 |
| FT | STRAND | 308 | 309 |
| FT | STRAND | 311 | 314 |
| FT | TURN | 318 | 319 |
| FT | STRAND | 321 | 325 |
| FT | STRAND | 332 | 332 |
| FT | STRAND | 337 | 340 |
| FT | TURN | 342 | 344 |
| FT | HELIX | 345 | 351 |
| FT | TURN | 352 | 354 |
| FT | STRAND | 361 | 365 |
| SQ | SEQUENCE | 365 AA; 40163 MW; EB48DFF24DF6A780 CRC64; | |

Query Match 80.0%; Score 32; DB 1; Length 365;
 Best Local Similarity 75.0%; Pred. No. 16;
 Matches 6; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
 |||:| ||
 Db 265 EVKVDGEF 272

RESULT 15

YFA0_ANASP

ID YFA0_ANASP STANDARD; PRT; 1906 AA.
 AC Q8YM40;
 DT 28-FEB-2003 (Rel. 41, Created)
 DT 28-FEB-2003 (Rel. 41, Last sequence update)
 DT 28-FEB-2003 (Rel. 41, Last annotation update)
 DE Hypothetical protein all5100 precursor.
 GN ALL5100.
 OS Anabaena sp. (strain PCC 7120).
 OC Bacteria; Cyanobacteria; Nostocales; Nostocaceae; Nostoc.
 OX NCBI_TaxID=103690;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=21595285; PubMed=11759840;
 RA Kaneko T., Nakamura Y., Wolk C.P., Kuritz T., Sasamoto S.,

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RA  Watanabe A., Iriguchi M., Ishikawa A., Kawashima K., Kimura T.,
RA  Kishida Y., Kohara M., Matsumoto M., Matsuno A., Muraki A.,
RA  Nakazaki N., Shimpo S., Sugimoto M., Takazawa M., Yamada M.,
RA  Yasuda M., Tabata S.;
RT  "Complete genomic sequence of the filamentous nitrogen-fixing
RT  cyanobacterium Anabaena sp. strain PCC 7120.";
RL  DNA Res. 8:205-213(2001).
CC  -!- SIMILARITY: BELONGS TO THE UPF0192 FAMILY.
CC  -----
CC  This SWISS-PROT entry is copyright. It is produced through a collaboration
CC  between the Swiss Institute of Bioinformatics and the EMBL outstation -
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CC  -----
DR  EMBL; AP003598; BAB76799.1; -.
DR  PIR; AD2443; AD2443.
DR  InterPro; IPR002890; A2M_N.
DR  Pfam; PF01835; A2M_N; 1.
KW  Hypothetical protein; Signal; Complete proteome.
FT  SIGNAL      1      25      POTENTIAL.
FT  CHAIN       26    1906      HYPOTHETICAL PROTEIN ALL5100.
SQ  SEQUENCE    1906 AA;  211372 MW;  B73C2F49C63EA92A CRC64;

  Query Match          80.0%;  Score 32;  DB 1;  Length 1906;
  Best Local Similarity 75.0%;  Pred. No. 79;
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Qy      1 EVKMDAEF 8
        |||:| ||
Db      736 EVKLDKEF 743

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Search completed: January 21, 2004, 09:23:07
Job time : 0.397706 secs